DOCOASAHEXAENOIC ACID

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The Brain Evolved in the Sea 500 Million Years Ago

Using DOCOSAHEXAENOIC ACID

PART I DARWIN:

“THE CONDITIONS OF EXISTENCE” IS THE MORE POWERFUL FORCE IN EVOLUTION

(IN ALL 6 EDITIONS OF THE ORIGIN!)

“We celebrate the past to awaken the future”

John F Kennedy

DHA WAS AND IS A CONDITION OF EXISTENCE


STAR FORMING REGION: - the stars in the Lynx arc are more than twice as hot as the Orion Nebula's central stars, with surface temperatures up to 80,000 degrees Celsius

PART II

A CONDITION OF EXISTENCE:

LIPIDS IN EVOLUTION

Synthesis of Arachidonic (AA) & Docosahexaenoic (DHA)

from LINOLEIC & α -LINOLENIC ACIDS

James Mead 1954, Rudolpho Brenner & Ralph Holman 1970s, Howard Sprecher, Norm Salem.

v.slow slow **AA**

18:2 ω6 ⇒ 18:3ω6 ⇒ 20:3ω6 ⇒ **20:4ω6** ⇔ **22:4ω6** ⇒ 22:5ω6

Linoleic ***Gamma-linolenic*** ⇓ ***Arachidonic***

seeds prostaglandins & leukotrienes

v.slow **EPA** slow **DHA** ⟶ Neuroprotectins

18:3ω3 ⇒ 18:4ω3 ⇒ 20:4ω3 ⇒ 20:5ω3 ⇒ **22:5ω3** **22:6 ω3**

Alpha-linolenic ***Eicosapentaenoic*** ⇓ ***Docosahexaenoic***

⇓ ⇑ **Peroxisomes**

leaves (photosynthesis) **24:5ω3** ⇒ 24:6ω3

v.slow

3 Billion Years Ago ⟶ Today

DNA? or RNA? PROTEINS

LIPIDS

Life Begins ca. 3 B Yrs before now > 600 - 500mya > 2007

Today

Oxygen

Anaerobic systems

Membrane lipids Trilobites

2.4 Billion years

Fish

Cyanobacteria

Amphibia

Reptiles

Stromatolites - blue green algae

Vendian "Cambrian Explosion"

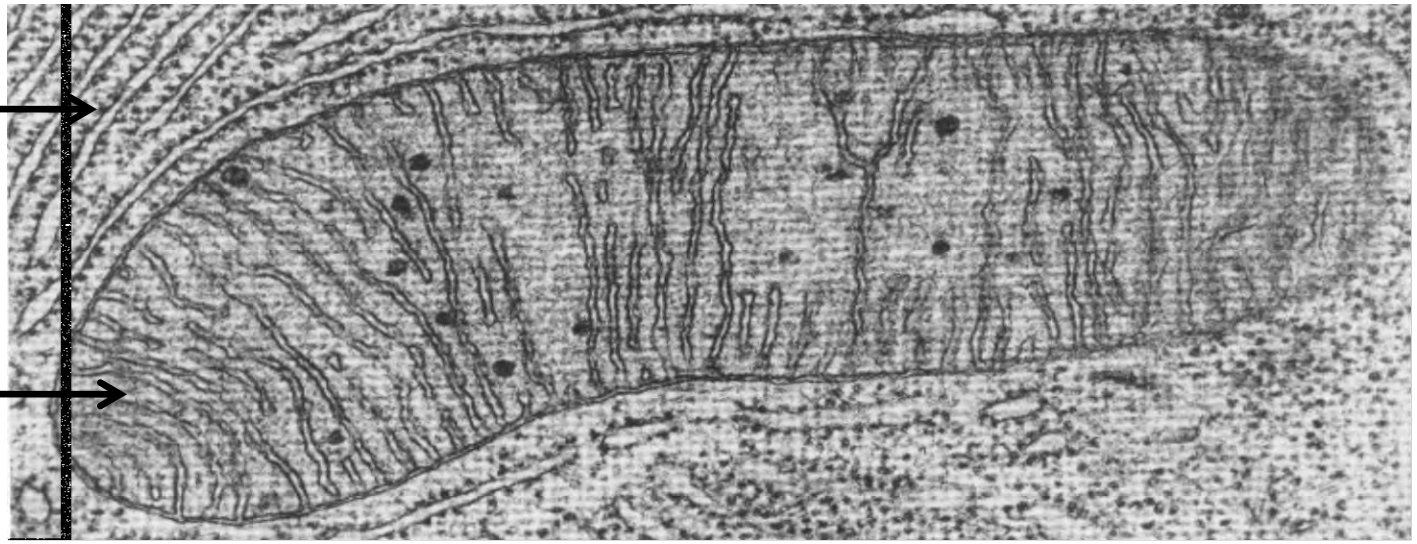
Mammals

Mainly Omega 3

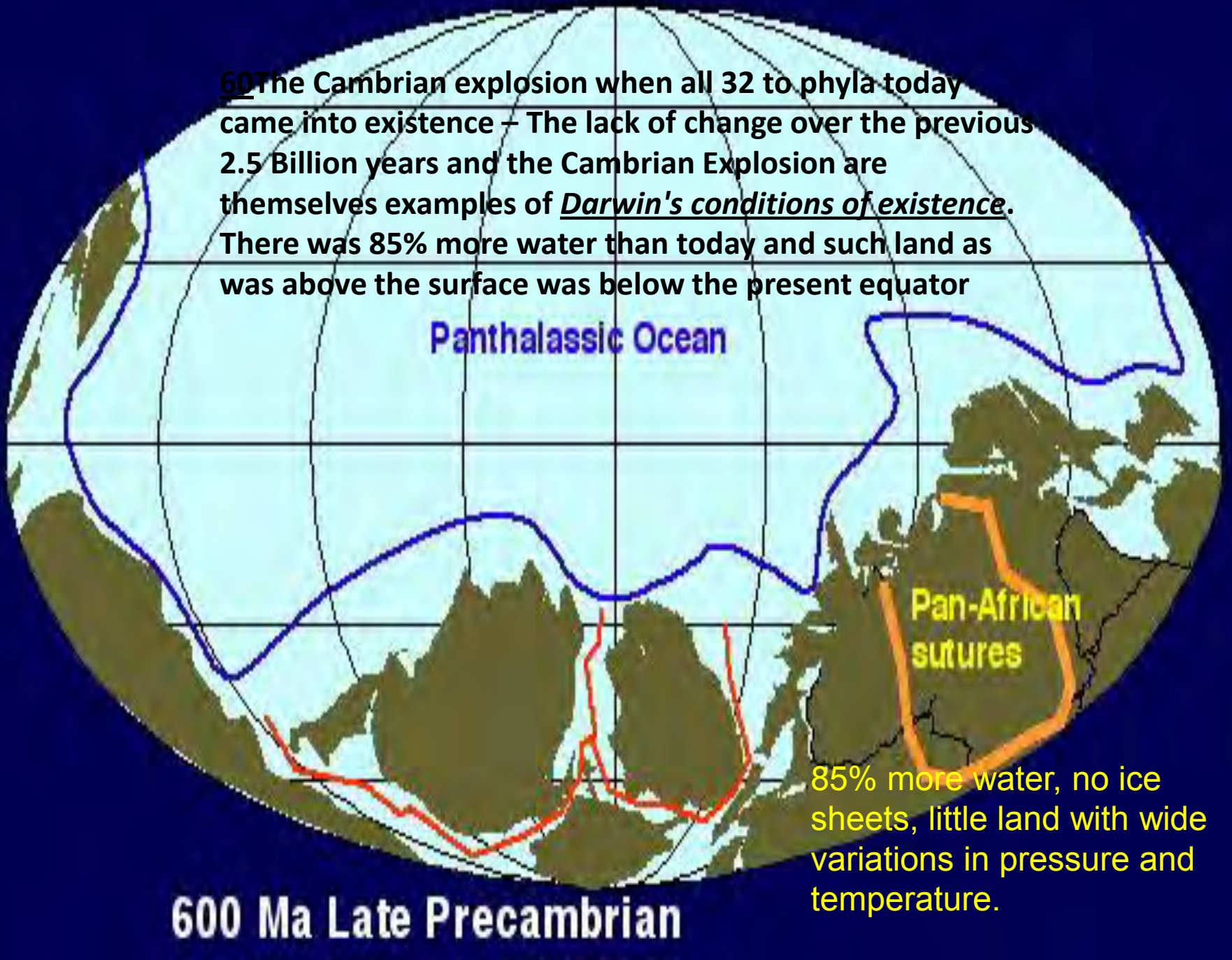
All 32 phyla come into existence

Lipid provided the intra and inter cell structure to create compartments and specialisation. They thus played a pivotal role in cell specialisation and speciation.

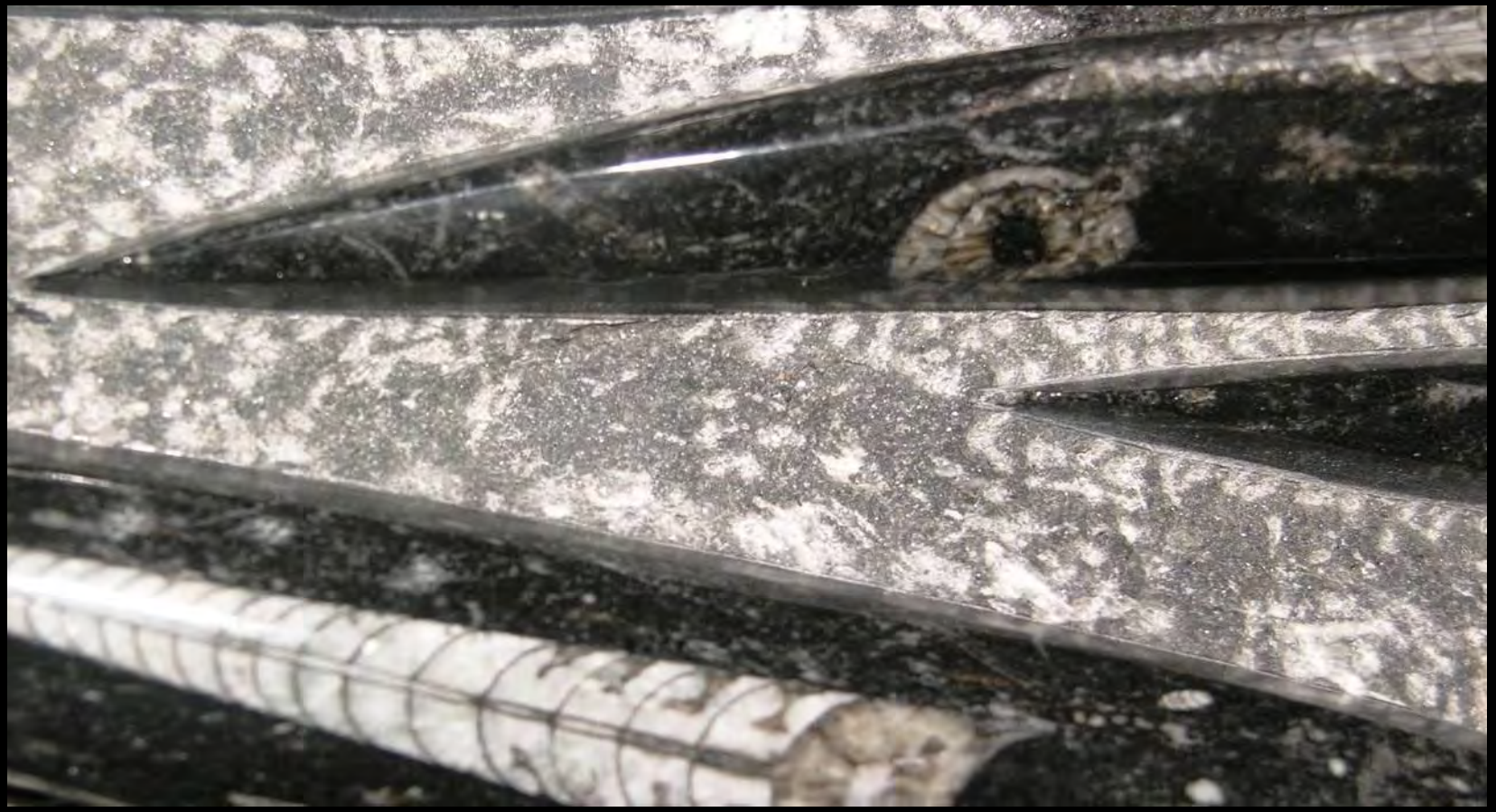
When oxygen became available in sufficient amount, complex molecules requiring high energy and oxygen were formed. Of these the lipids played an important role forming the cell membranes making intracellular compartmentalisation and specialisation possible.



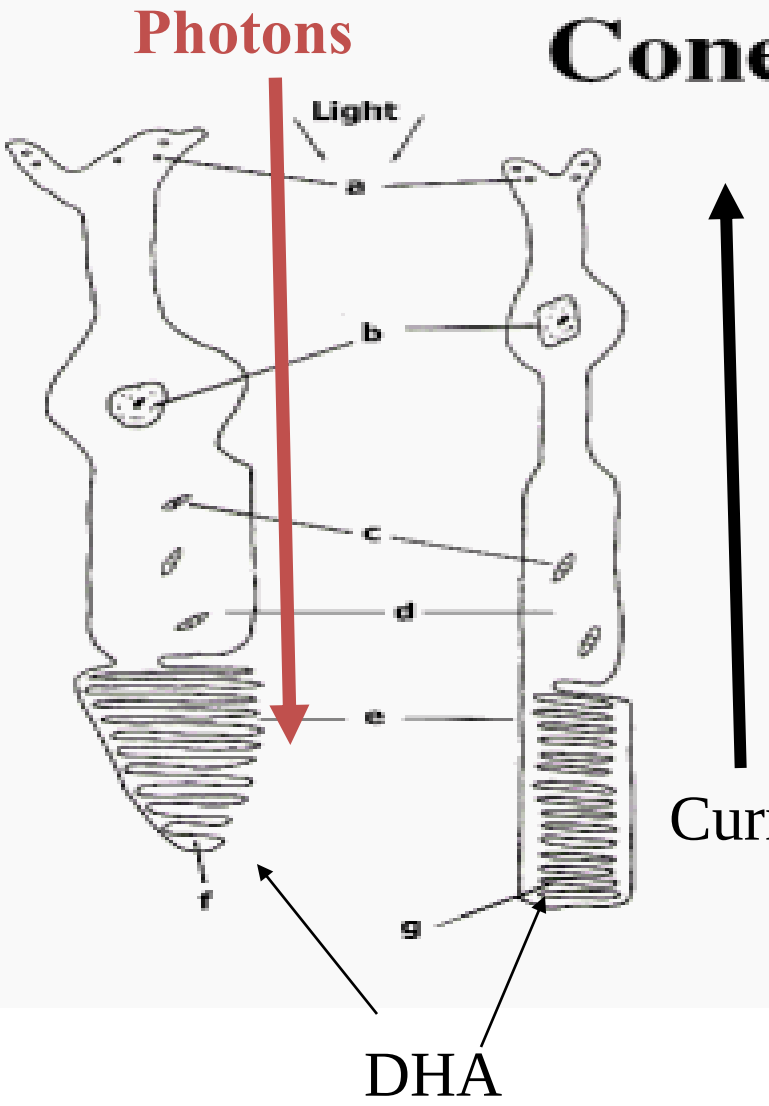
Intracellular specialisation led to specialisation of the cells themselves and eventually speciation.


60The Cambrian explosion when all 32 to phyla today came into existence – The lack of change over the previous 2.5 Billion years and the Cambrian Explosion are themselves examples of *Darwin's conditions of existence*. There was 85% more water than today and such land as was above the surface was below the present equator
Panthalassic Ocean
Pan-African sutures
85% more water, no ice sheets, little land with wide variations in pressure and temperature.
600 Ma Late Precambrian

The Eye of Orthocerus looking at you from 450 million years ago



Cells in the sensory retina: Rods and Cones - IV



Legend:

a: vesicle

b: nucleus

c: mitochondrion

d: inner segment

e: outer segment

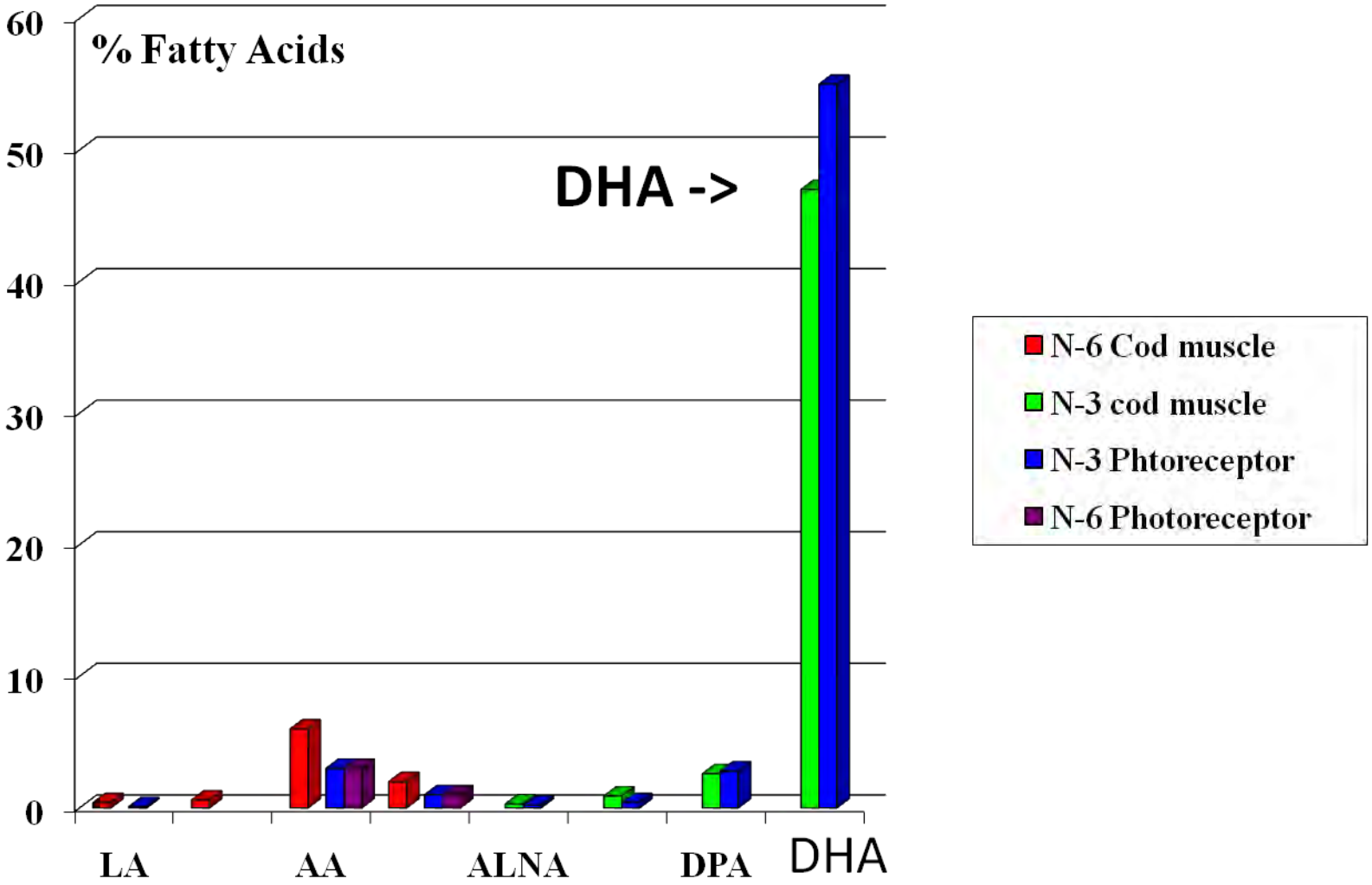
f: "discs" containing iodopsin

g: discs containing rhodopsin

Turns light into electricity

Six oxygens are required for the six double bonds alone

Photo-receptor Omega 3 requirement as DHA.
Ethanolamine Phosphoglycerides –
Gene Anderson & Nicholas Bazan 1968-74



PART III

That DHA influences gene expression is further evidence for its role in cerebral expansion leading to H. sapiens.

Ligand activity for nuclear receptors

- MD studies: DHA as a structural analog of the retinol molecule, 11-12 zig zag carbons of length = naturally folded DHA.

- AA - PKC activation [1] NF-kappaB and PPARs - a PPAR ligand [2]
  Heart Mn SOD(3)

- DHA is a natural ligand for RXR [4] – obligatory step – stimulates > 107 genes (5,6)

AA endothelium,

1. **Hindenes** *JO, Nerdal W, Guo W, Di L, Small DM, Holmsen H (2000) Physical properties of the transmembrane signal molecule, sn-1-stearoyl 2-arachidonoylglycerol. Acyl chain segregation and its biochemical implications. J Biol Chem. 275(10): 6857-6867.*
2. **Alaoui-El-Azher** *M, Wu Y, Havet N, Israel A, Lilienbaum A, Touqui L. (2002) Arachidonic acid differentially affects basal and lipopolysaccharide-induced sPLA(2)-IIA expression in alveolar macrophages through NF-kappaB and PPAR- gamma-dependent pathways. Mol Pharmacol 61(4):786-94.3.*
3.. **Phylactos,** *A., Harbige L.S., Crawford, M.A. (1994) Essential fatty acids alter the activity of manganese superoxide dismutase in rat heart. Lipids 29: 111 115.*

DHA neural system

4. **de Urquiza** *AM, Liu S, et al (2000) Docosahexaenoic acid, a ligand for the retinoid X receptor in mouse brain Science. 290(5499): 2140-2144.*
5. **Ikemoto** *A, Nitta A, Furukawa S, Ohishi M, Nakamura A, Fujii Y, Okuyama H. (2000) Dietary n-3 fatty acid deficiency decreases nerve growth factor content in rat hippocampus. Neurosci Lett. 285: 99-102.*
6. **Kitajka** *K, Puskas LG, Zvara A, Hackler L Jr, Barcelo-Coblijn G, Yeo YK, Farkas T. (2002) The role of n-3 polyunsaturated fatty acids in brain: modulation of rat brain gene expression by dietary n-3 fatty acids. Proc Natl Acad Sci U S A; 99(5):2619-24.*

Gene expression by brain DHA

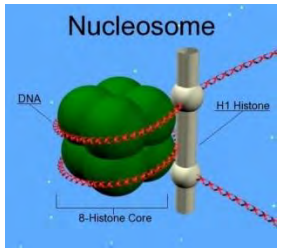
. Kitajka K, Sinclair AJ, Weisinger RS, Weisinger HS, Mathai M, Jayasooriya AP, Halver JE, Puskás LG.(2004) Effects of dietary omega-3 polyunsaturated fatty acids on brain gene expression Proc Natl Acad Sci U S A.;101(30):10931-6

- Lipid metabolism 4
- Membrane proteins 5
- Endocytosis, synaptic vesicle recycling, formation. 4
- Synaptic proteins 2
- Cytoskeleton 7
- Signal transduction 11
- Others 16

Some Genes influenced by DHA > 4 fold.

. Kitajka K, Sinclair AJ, Weisinger RS, Weisinger HS, Mathai M, Jayasooriya AP, Halver JE, Puskás LG.(2004) Effects of dietary omega-3 polyunsaturated fatty acids on brain gene expression Proc Natl Acad Sci U S A.;101(30):10931-6

- Serine palmitoyl transferase > 5 membrane receptor function.
- Farnesyl pyrophosphate syn. (testis)
- Sec24 prot. (Sec24A isoform). mediates protein transport from the endoplasmic reticulum AJ131244
- Clathrin-ass. adaptor chain mu 1A recognition and intracellular transport of many membrane proteins to epithelial cells AF139405
- Ubiquitin-prot. ligase Nedd4-2 ubiquitin ligase is involved in polyubiquitination removal of protiens
- Elongation factor 1-alpha X63561 responsible for the enzymatic delivery of aminoacyl tRNAs to the ribosome.
- Beta-globin for heme construction in mitochondria (energy).
- Parathyroid hormon reg. sequence AA290355
- Ribosomal prot. L7a Silences transcription in absence and amplifies in presence of ligands
- U1 small nuclear ribonucleoprot. Hom AW189878 Anti autoimmunity.

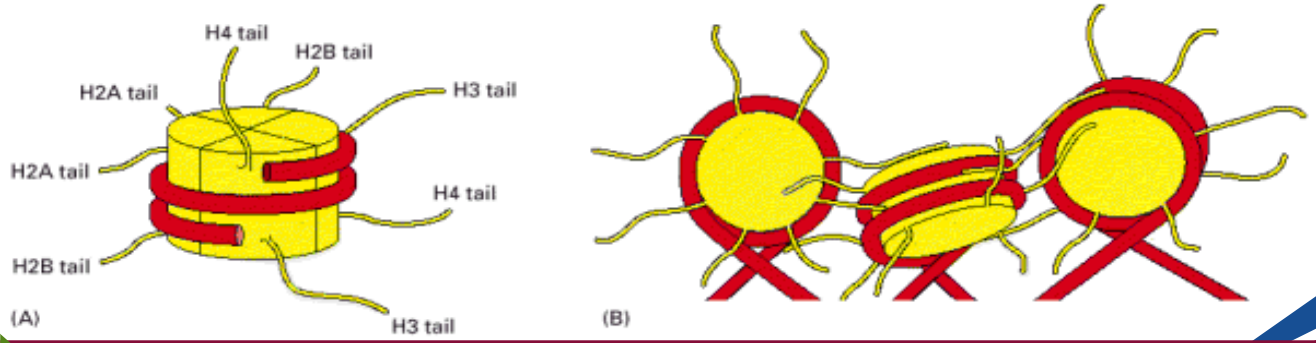


Histones

A. J. Sinclair

- chief protein component of chromatin
- act as spools around which DNA winds (forming nucleosome)
- histone (+) and DNA (-) : help to compact DNA
- four **core histone** : H2A, H2B, H3 and H4
- the **linker histone** : H1
- they play a role in gene regulation

  - core histone tail modification regulates DNA compaction
  - undergo post-translational modification
  - histones may be a key factor in turning specific genes on or off (epigenetics)

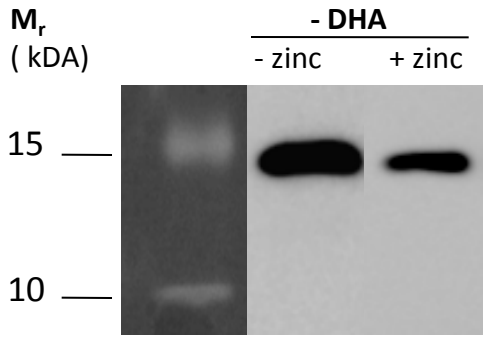


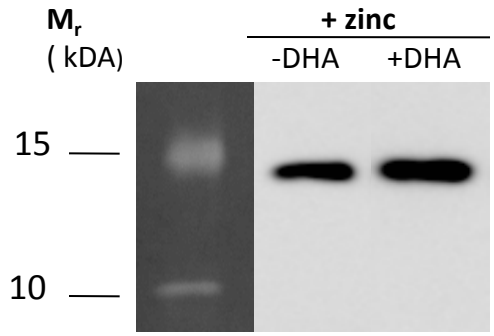
Results

Western blot analysis

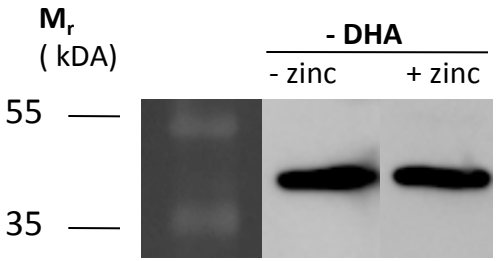
DEAKIN UNIVERSITY AUSTRALIA

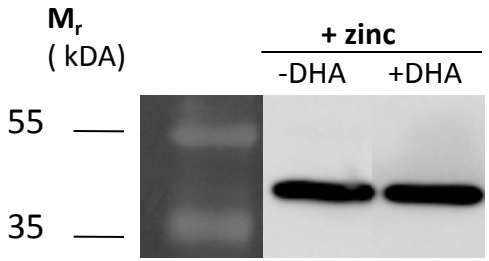
A.J.SINCLAIR



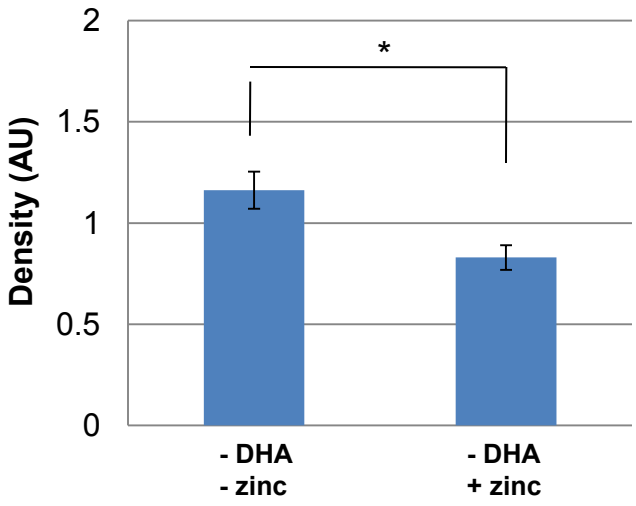


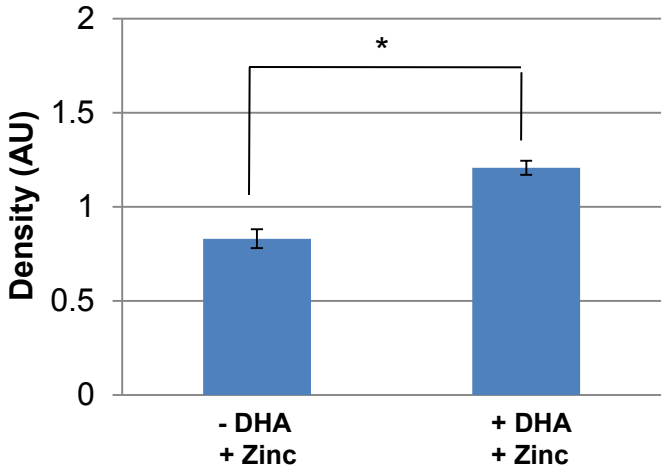
(A). H3





(B). β actin

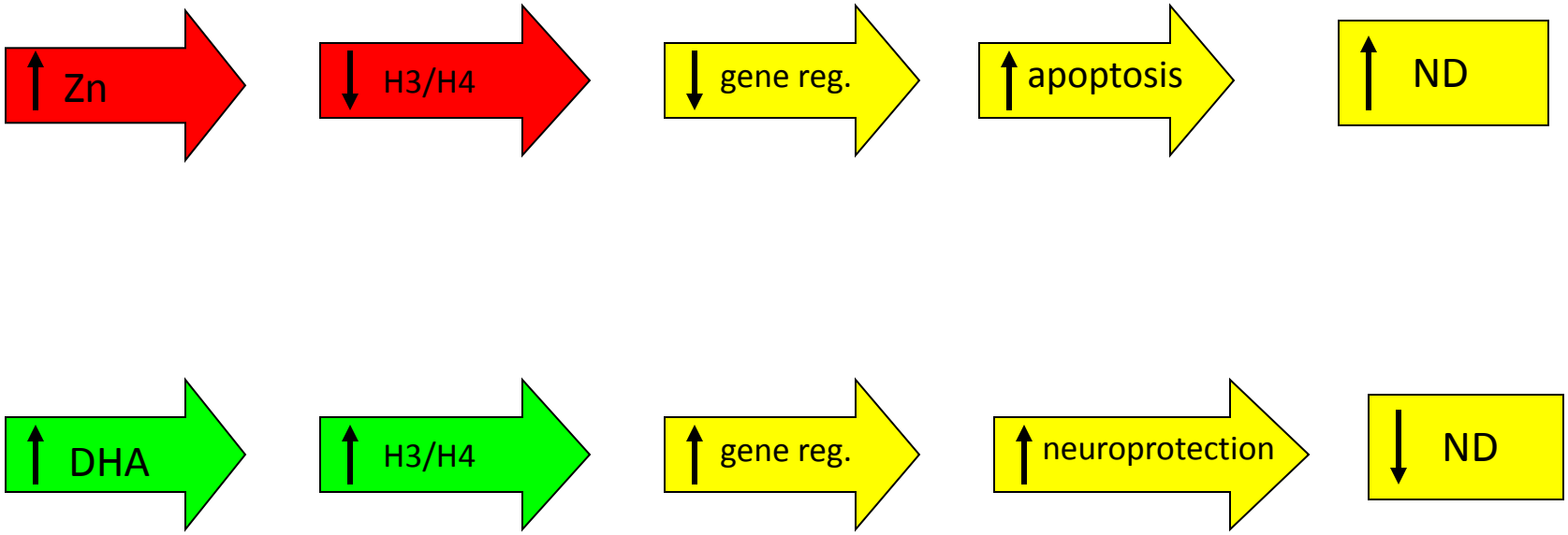




(C). Densitometry analysis

Using monoclonal antibodies specific to human histone H3A and H4B

Key findings and potential outcomes

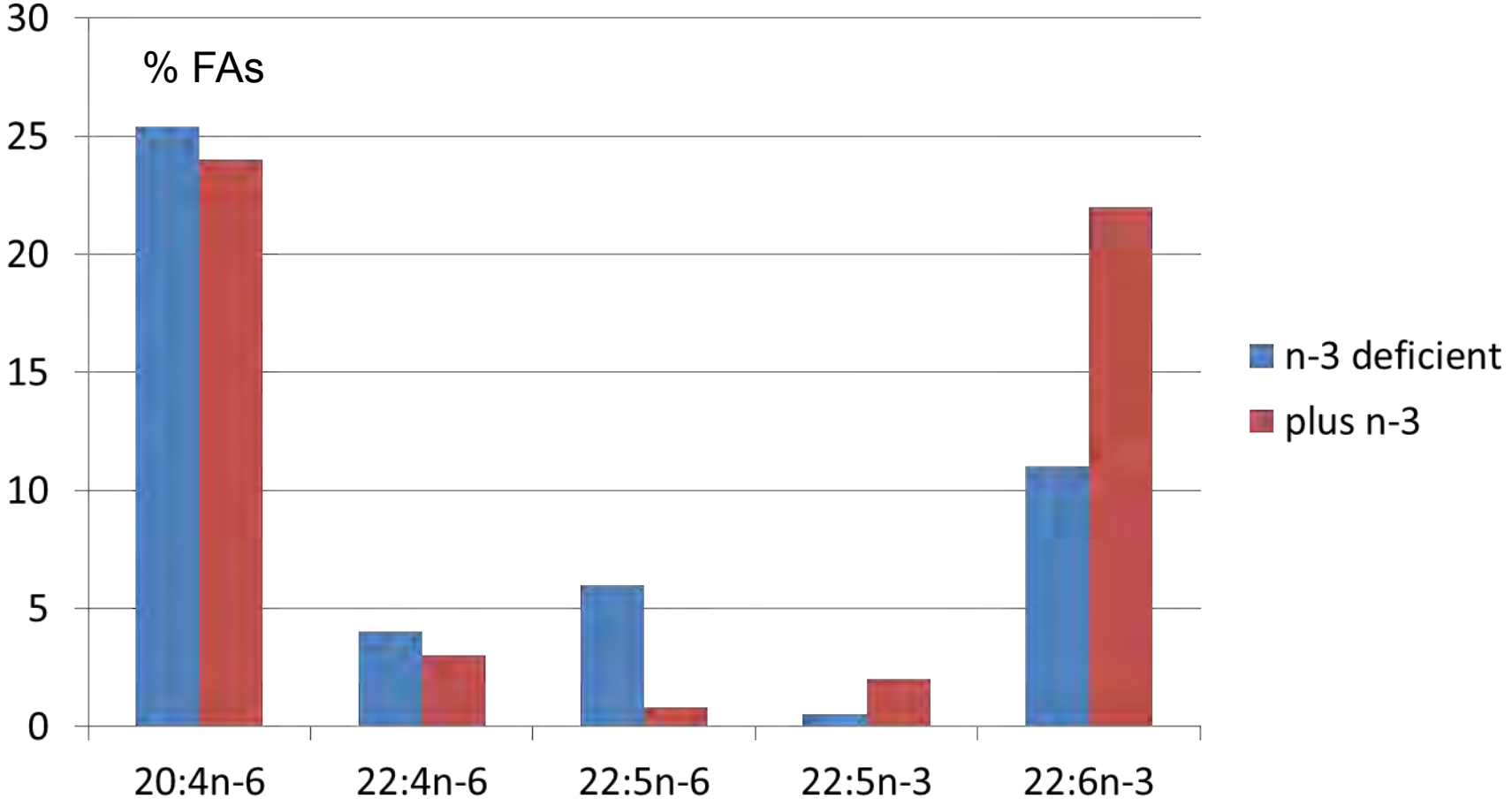


Conclusions

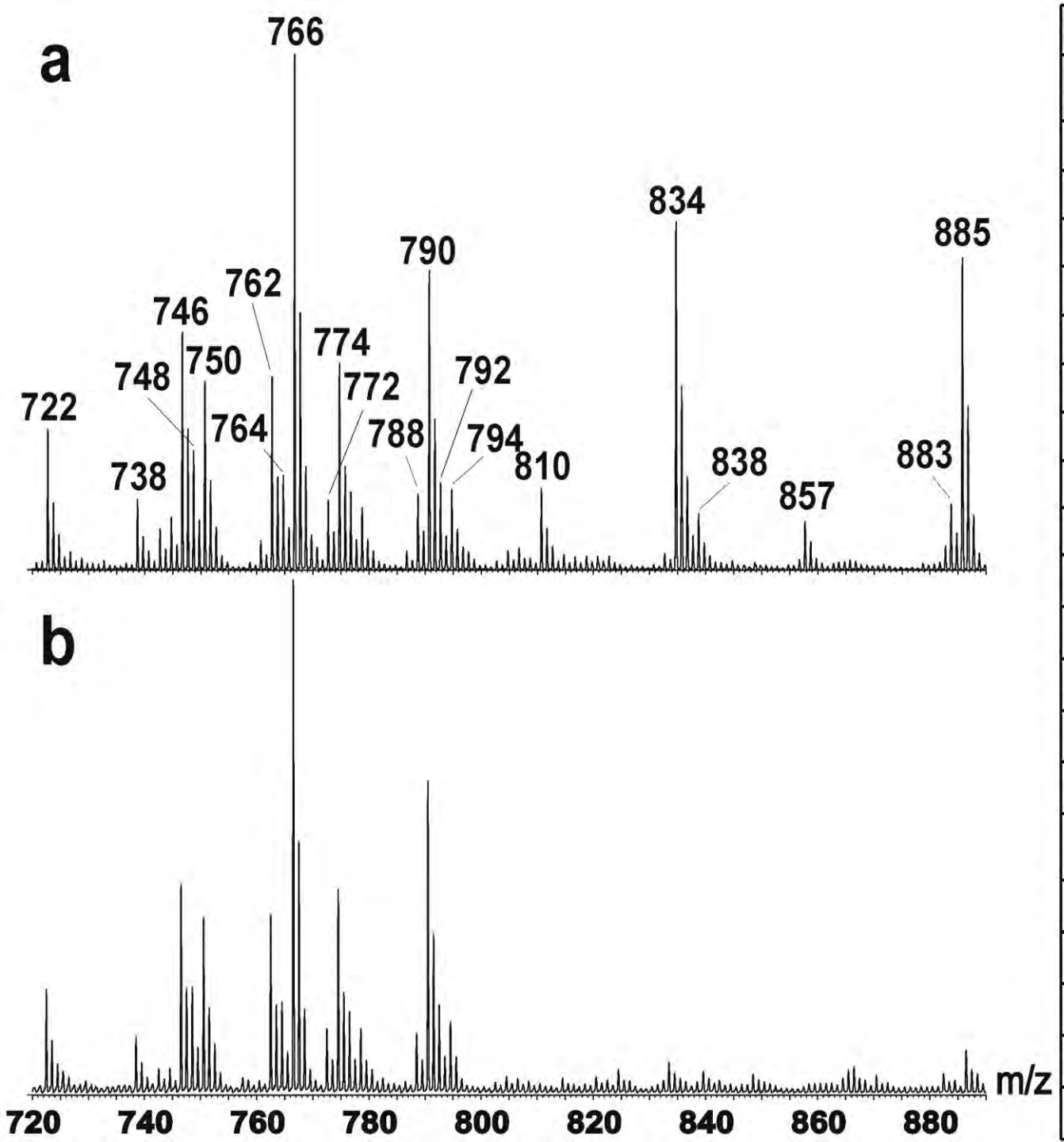
- Zinc and DHA may cause global effect on gene expression, mediated by histones (epigenetics)
- Zinc and DHA play important role in neuroprotection:
  - synergistically by modulating gene and protein expression, and critically
  - via survival signaling pathways
- May contribute to future treatment and prevention of neurodegenerative diseases

With thanks to A. J. Sinclair

Rat pup brain LCPufas with maternal diet with and without n-3.

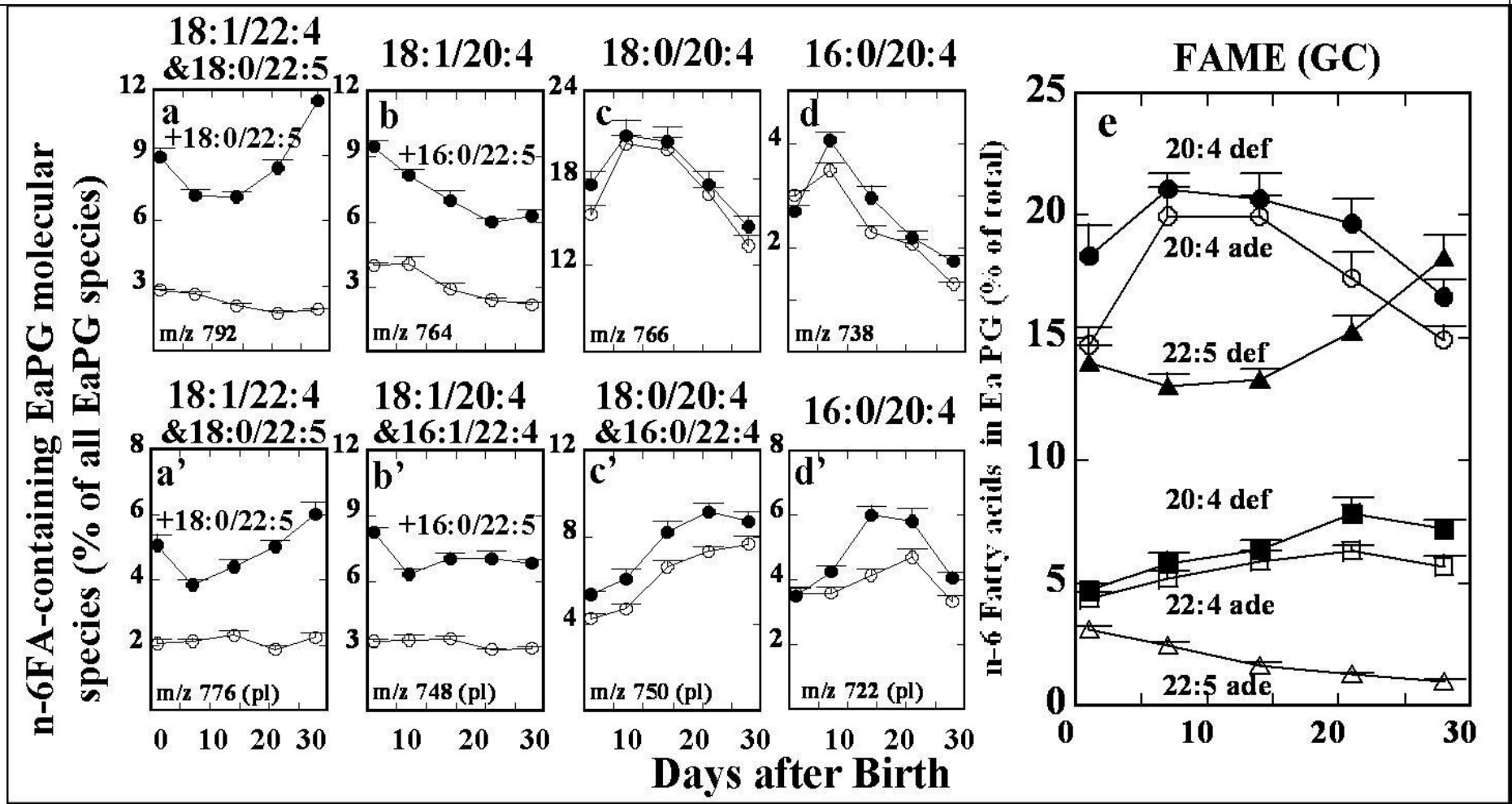


Brand A, Crawford MA, Yavin E. (2010) Retailoring docosahexaenoic acid-containing phospholipid species during impaired neurogensis following omega-3 alpha-linolenic acid deprivation. J Neurochem. 114(5):1393-404.

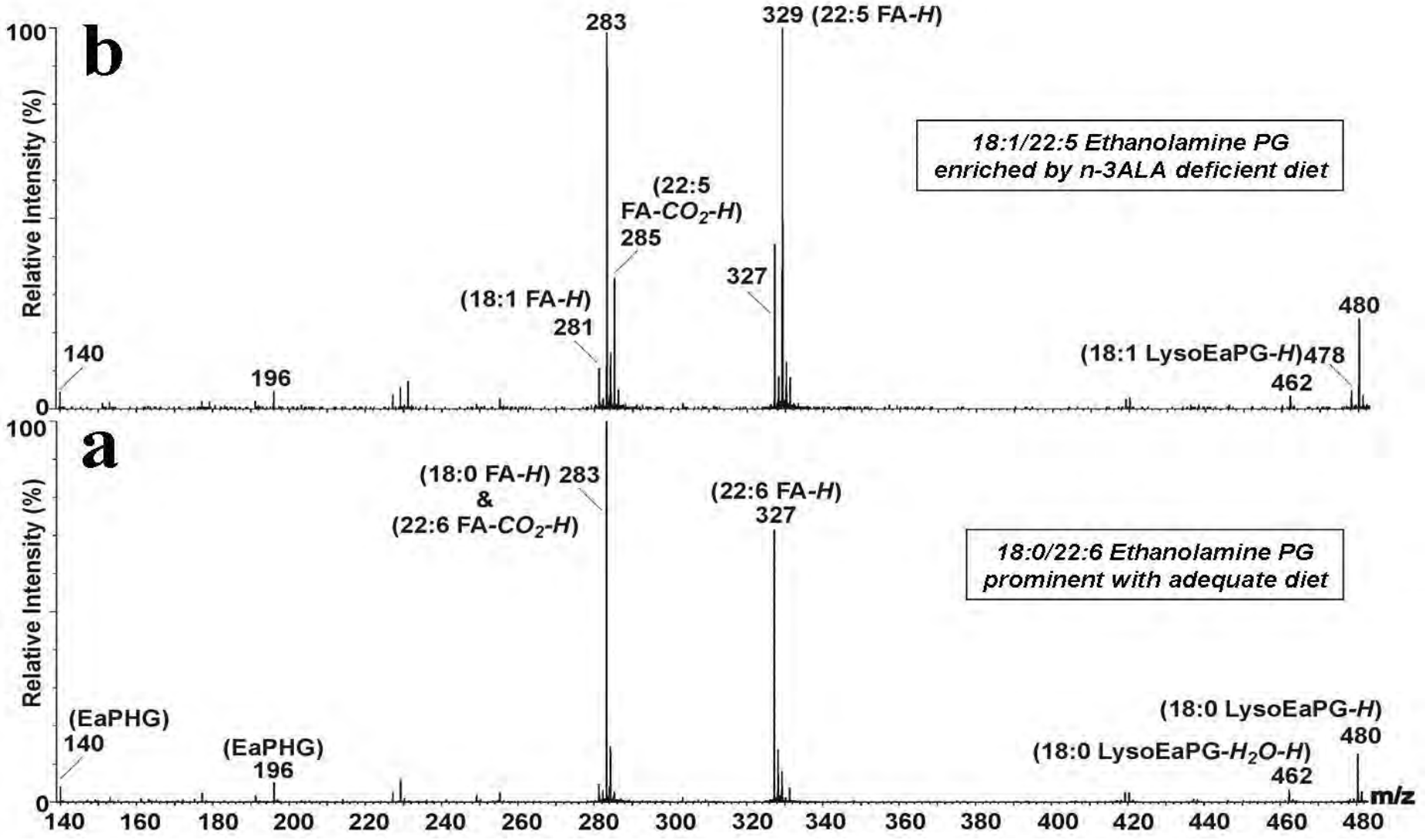


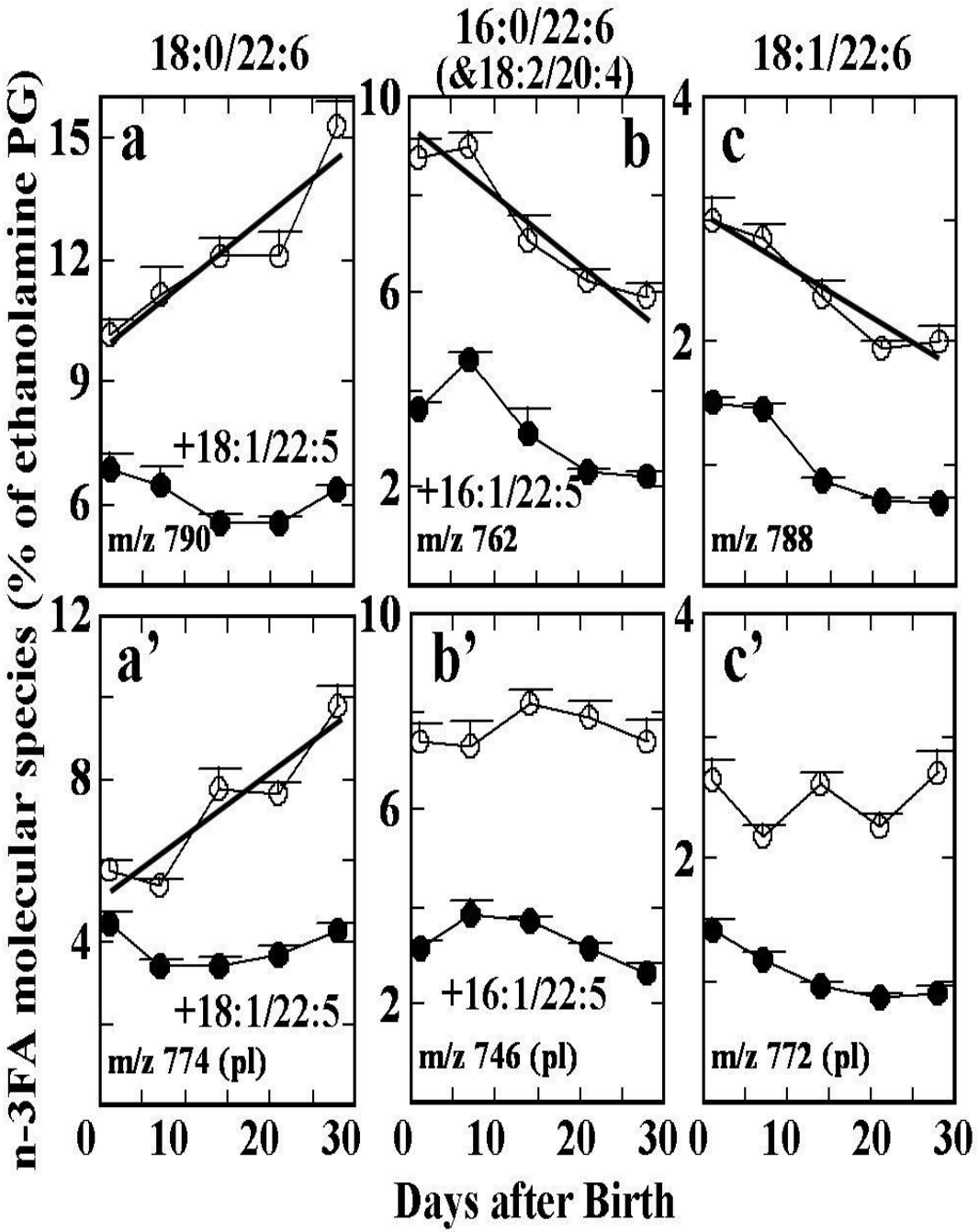
Peak assignments		
m/z	*PG class*	*Long chain pairing*
722	EapPG	16:0/20:4
738	EaPG	16:0/20:4
746	EapPG	16:0/22:6; 18:2/20:4
748	EapPG	18:1/20:4; 16:1/22:4
750	EapPG	16:0/22:4; 18:0/20:4
762	EaPG	16:0/22:6; 18:2/20:4
764	EaPG	18:1/20:4
766	EaPG	18:0/20:4
772	EapPG	18:1/22:6
774	EapPG	18:0/22:6
788	EaPG	18:1/22:6
790	EaPG	18:0/22:6
792	EaPG	18:1/22:4; 18:0/22:5
794	EaPG	18:0/22:4
810	SerPG	16:0, 22:4/18:0, 20:4
834	SerPG	18:0,22:6/18:1,22:5
838	SerPG	18:0/22:4
857	InsPG	16:0/20:4
883	InsPG	18:1/20:4
885	InsPG	18:0/20:4

Time course of molecular species' changes in the major n-6 fatty acid containing 1,2-diacyl-EaPG (panels a-d) and 1-alk,2-acyl-EaPG (panels a'-d') (ESI/Q-Tof analysis) and total ethanolamine fatty acids (panel e) (GC analysis) in the developing postnatal cortex. Open circles represent the adequate diet and closed circles represent n-3ALA-deficient groups. Molecular weight annotations (m/z) are depicted in the graphs. Plasmalogen species (1-alk,2-acyl-EaPG).



Tandem ESI/MS (Q-TOF) of EaPG species. Product-ion spectra of the $[M-H]^-$ ion at m/z 790.5. Lipid extracts were injected directly into the ESI/Q-Tof mass spectrometer. For each spectrum 2 min of signal averaging was employed and the collision energy was 30 eV. EaPHG, ethanolamine polar headgroup; FA fatty acid; LysoEaPG, lyso-EaPG.





DHA BEHAVIOUR:

Time course of molecular species changes in the major n-3 fatty acid containing 1,2-diacyl-EaPG (panels a-c) and 1-alk,2-acyl-EaPG (panels a'-c') in the developing postnatal cortex. Lipid extracts were injected directly into the ESI/Q-TOF mass spectrometer. Values (% ±SEM) were obtained from 3-5 pregnant dams (n = 6 pups). All differences between adequate (open circles) and deficient (closed circles) groups are significant with a p-value <0.05 using the non-parametric Mann-Whitney test. Molecular weight annotations (m/z) are depicted in the graphs. Abbreviations: pl, plasmalogen species (1-alk, 2-acyl-EaPG).

NOTE HOW

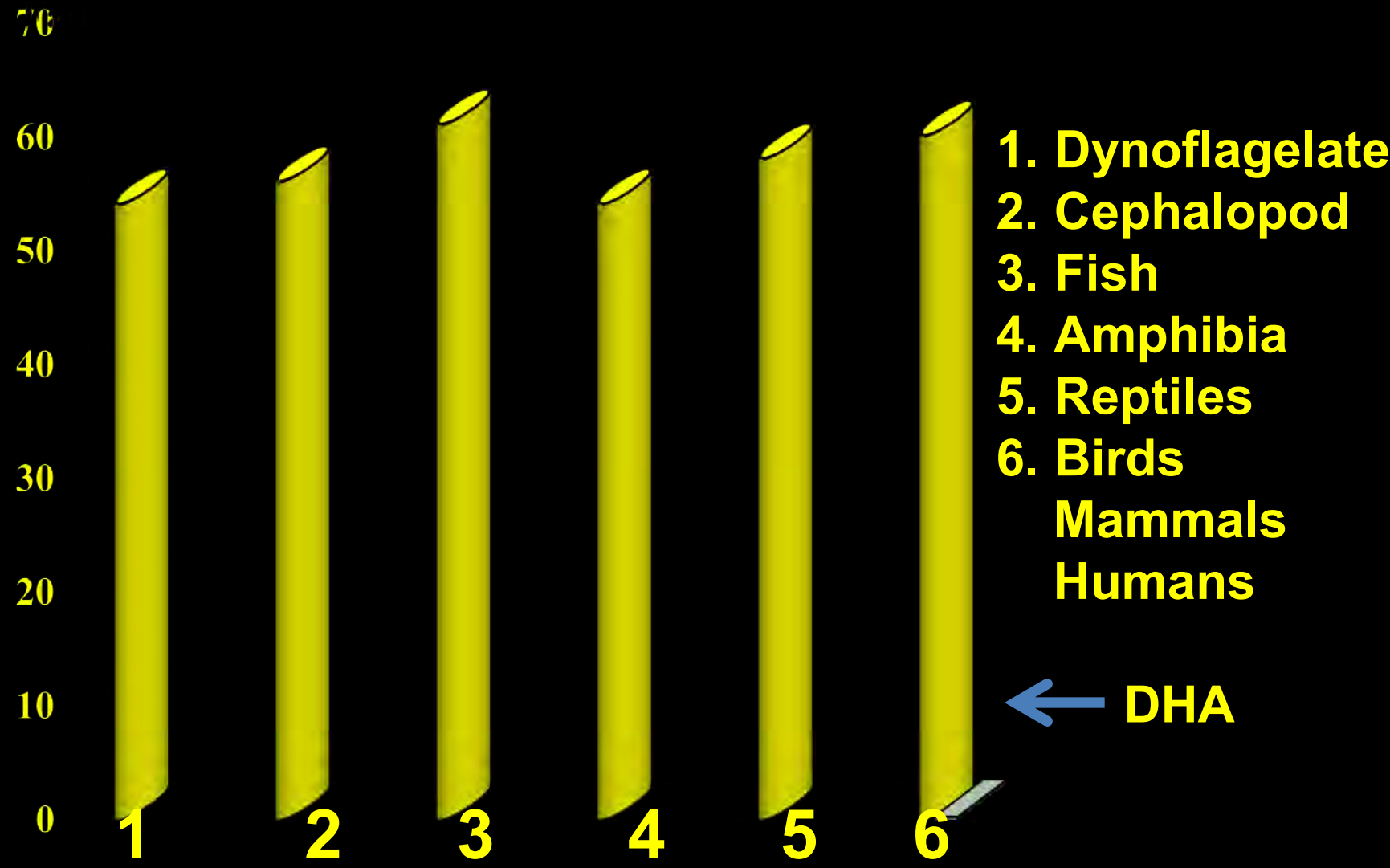
1. 18:0-20:4 IS UNINFLUENCED BY THE Ω3 DEFICIENCY.

2. THE 18:0-22:6 INCREASES WITH TIME

BUT 18:1-22:6 DIMINISHES.

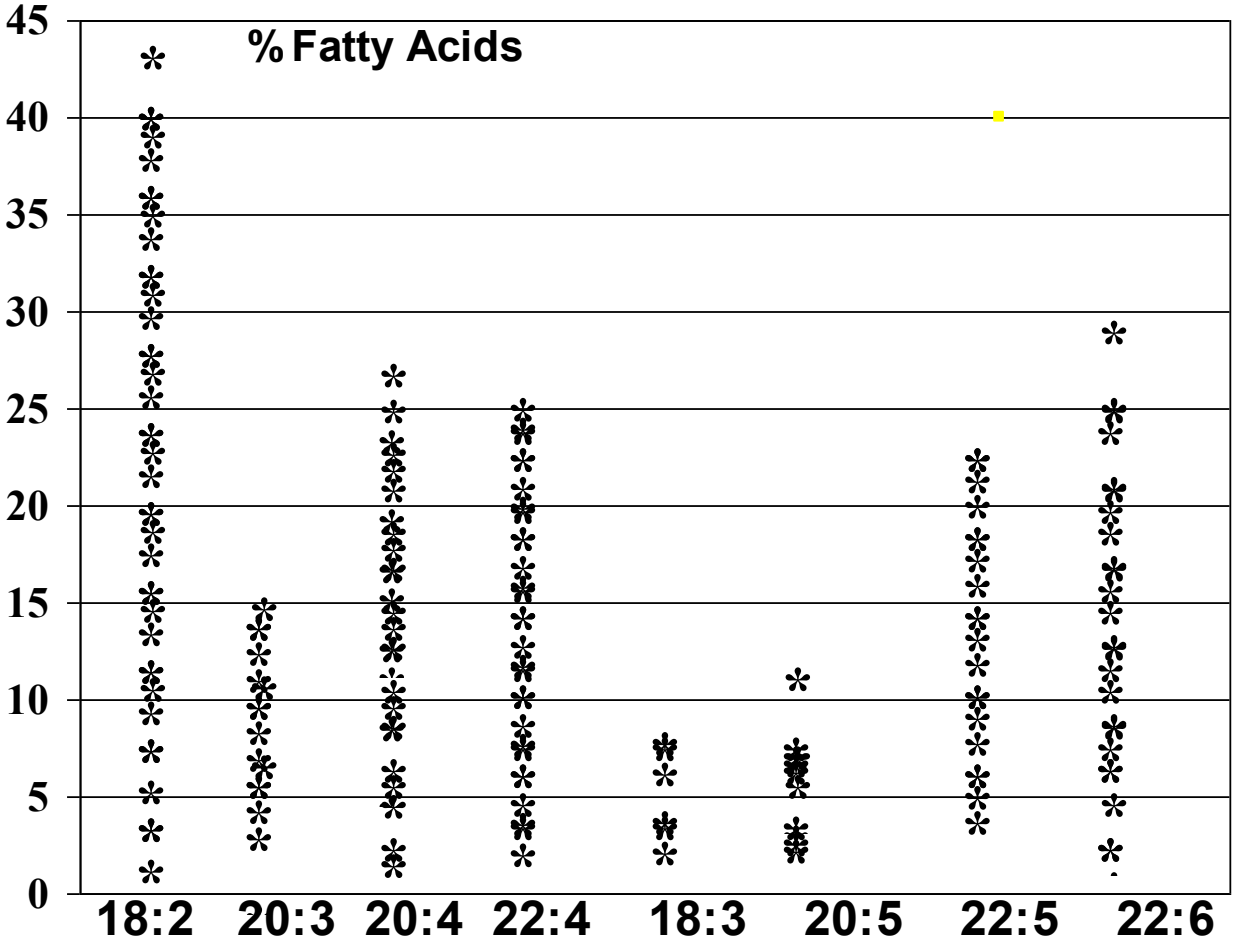
BRAND A, CRAWFORD MA, YAVIN E. (2010) RETAILORING DOCOSAHEXAENOIC ACID-CONTAINING PHOSPHOLIPID SPECIES DURING IMPAIRED NEUROGENSIS FOLLOWING OMEGA-

From the eye spot of the dynoflagelate to mammals, the chemistry is the same over 600 M Years of evolution (Bazan & Anderson).



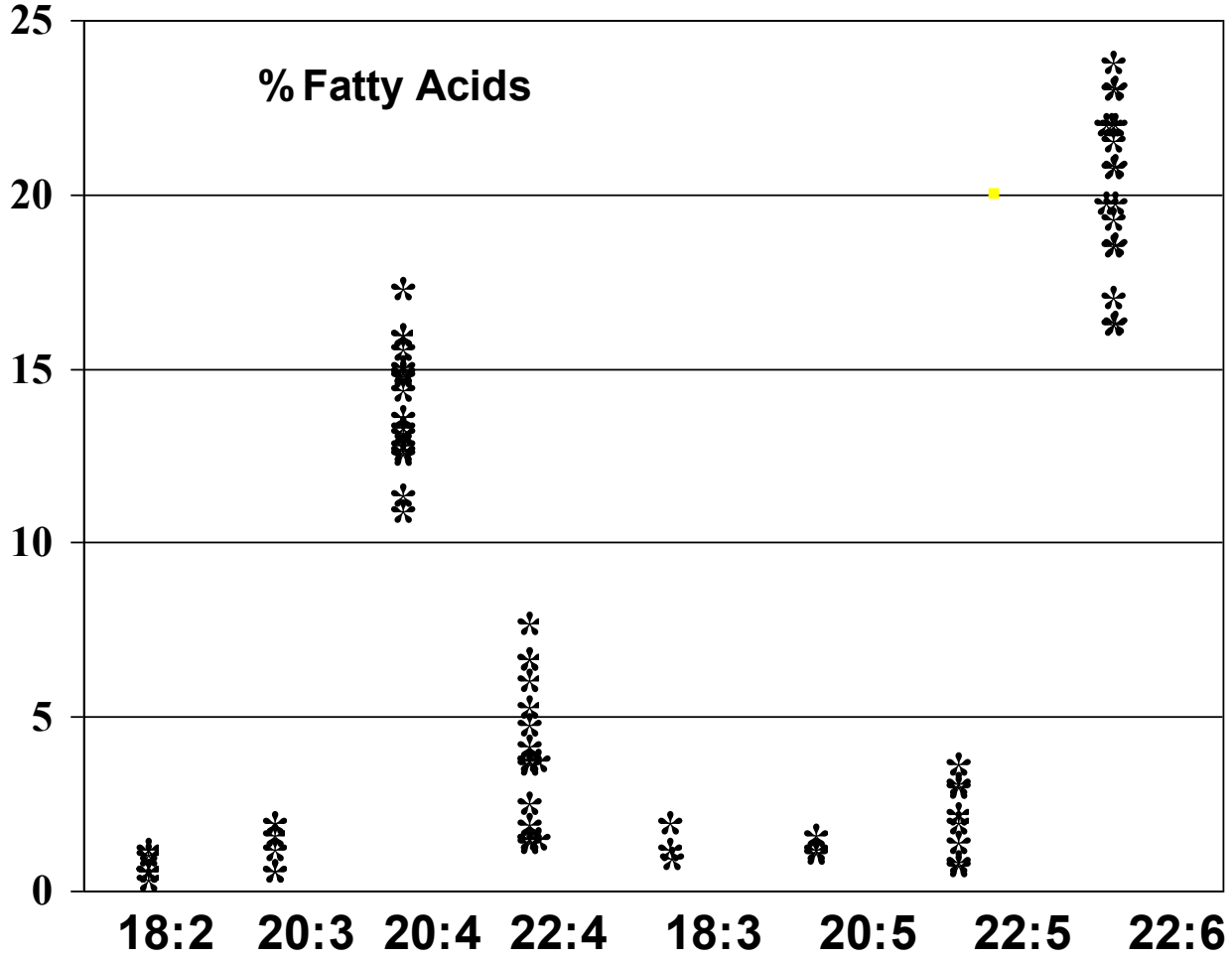
The most compelling evidence for essentiality for DHA

Liver Essential Fatty Acid Composition
Ethanolamine Phosphoglycerides: 42 species



Crawford M, Casperd N. Sinclair AJ (1976) The long chain metabolites of linoleic and linolenic acids in liver and brain in herbivores and carnivores. Comp. Biochem. Physiol. 54B: 395-401.

Brain Essential Fatty Acid Composition
Ethanolamine Phosphoglycerides: 42 species

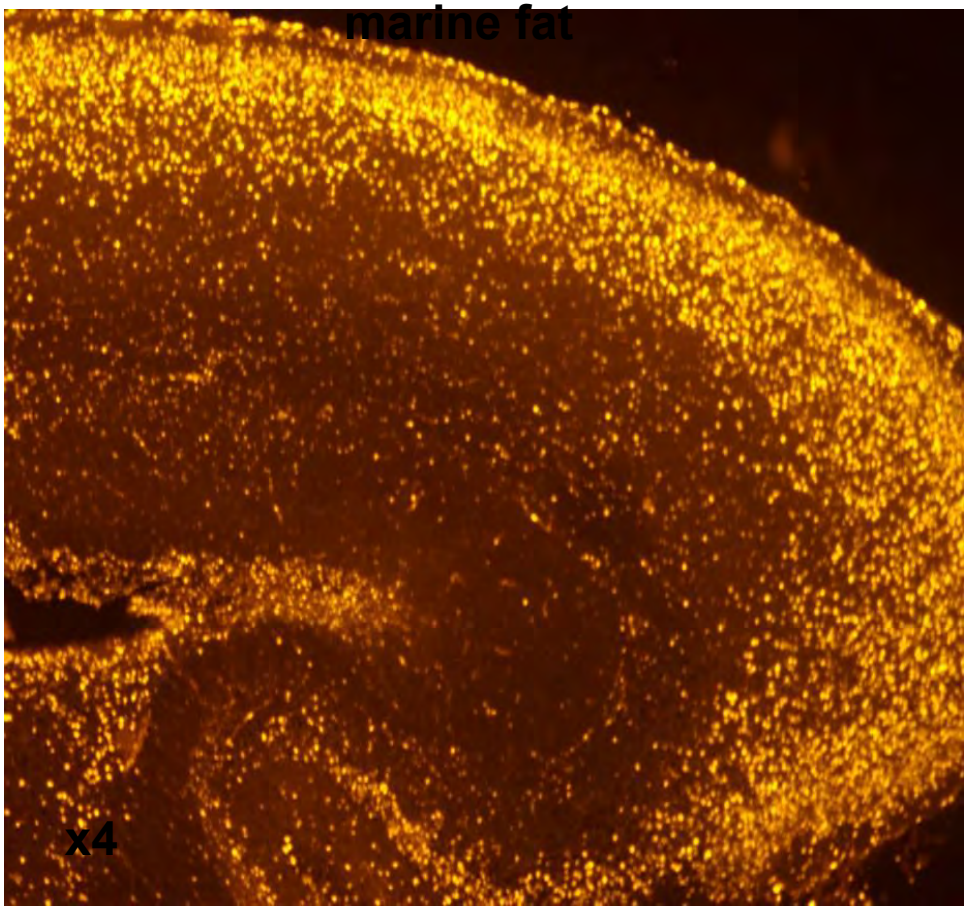


Crawford M, Casperd N. Sinclair AJ (1976) The long chain metabolites of linoleic and linolenic acids in liver and brain in herbivores and carnivores. Comp. Biochem. Physiol. 54B: 395-401.

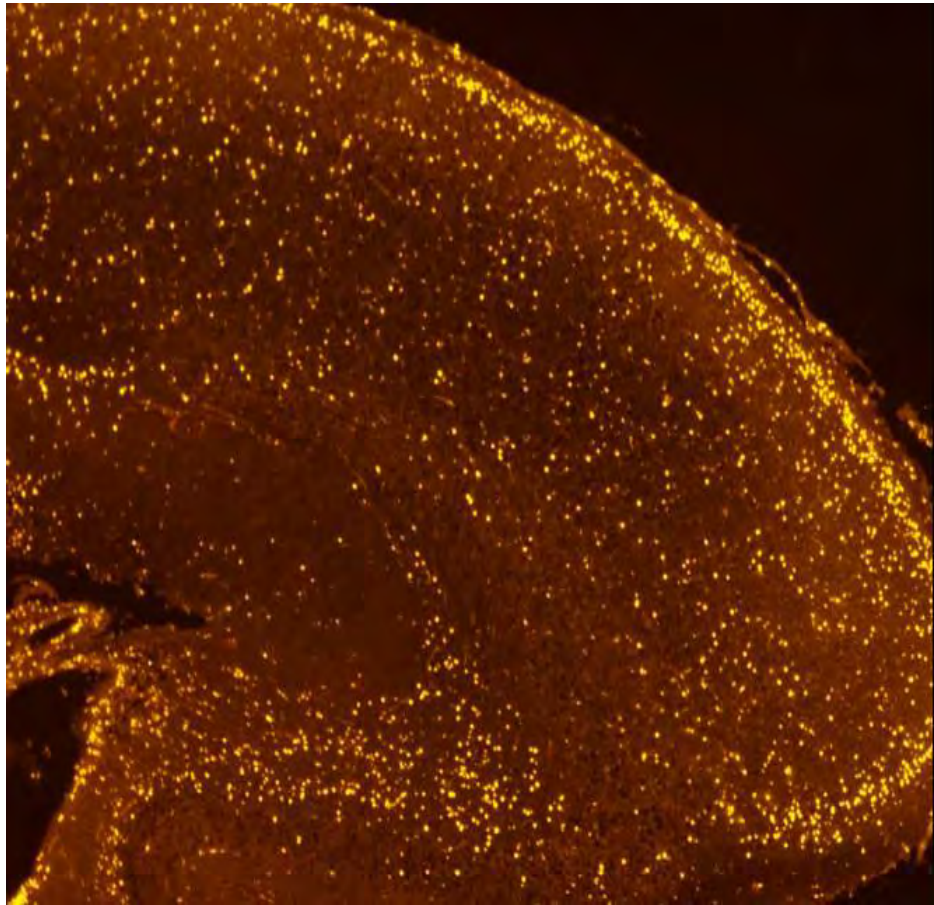
DHA deficiency (of marine fat) in the developing brain restricts migration of cortical neurones.

Yavin E., Himovichi E. and Eilam R. (2009) Delayed cell migration in the developing rat brain following maternal Omega 3 alpha linolenic acid dietary deficiency. Neuroscience 162, 1011–1022.

Maternal Diet 59 with marine fat



Diet 61 (Deficient)

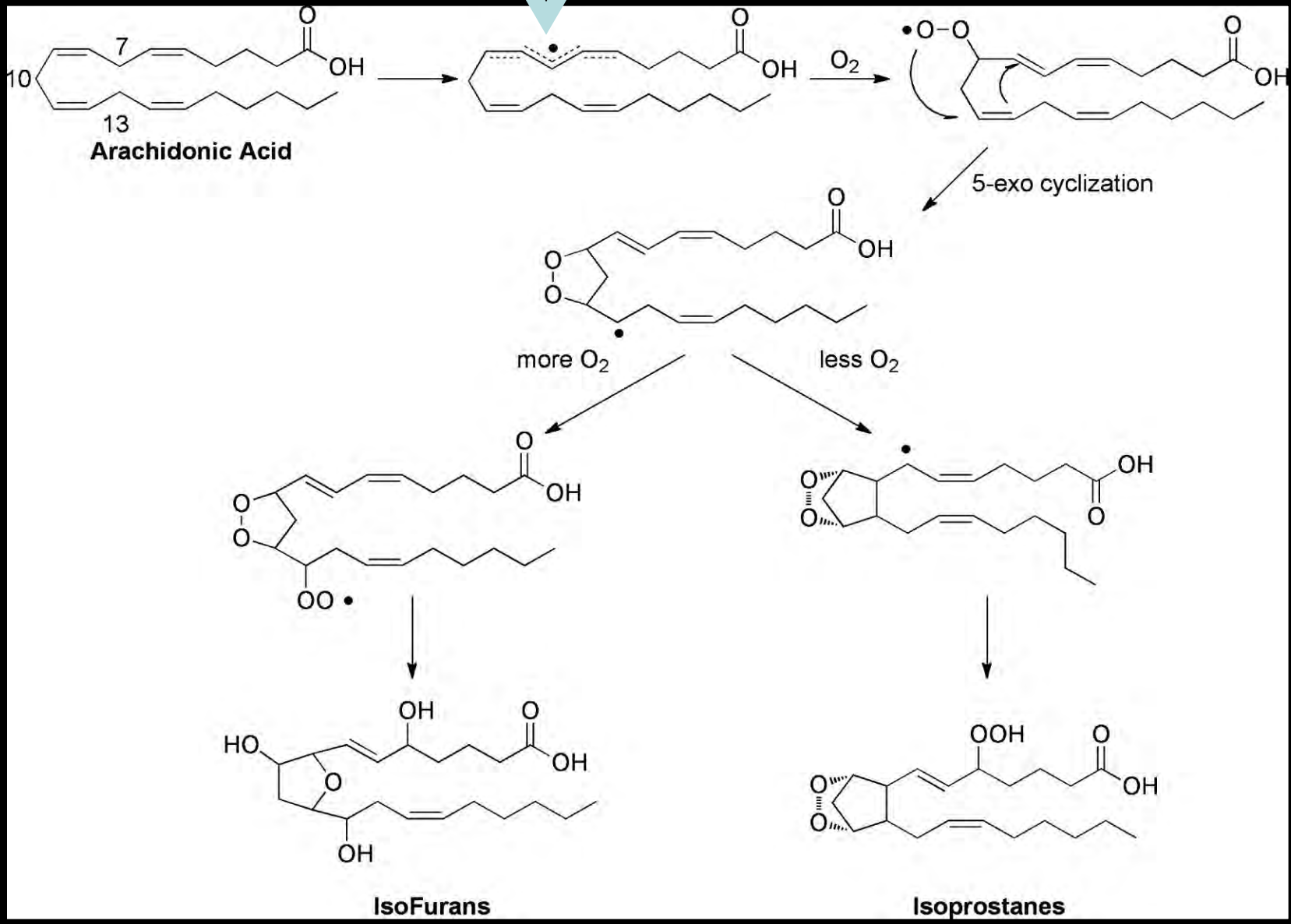


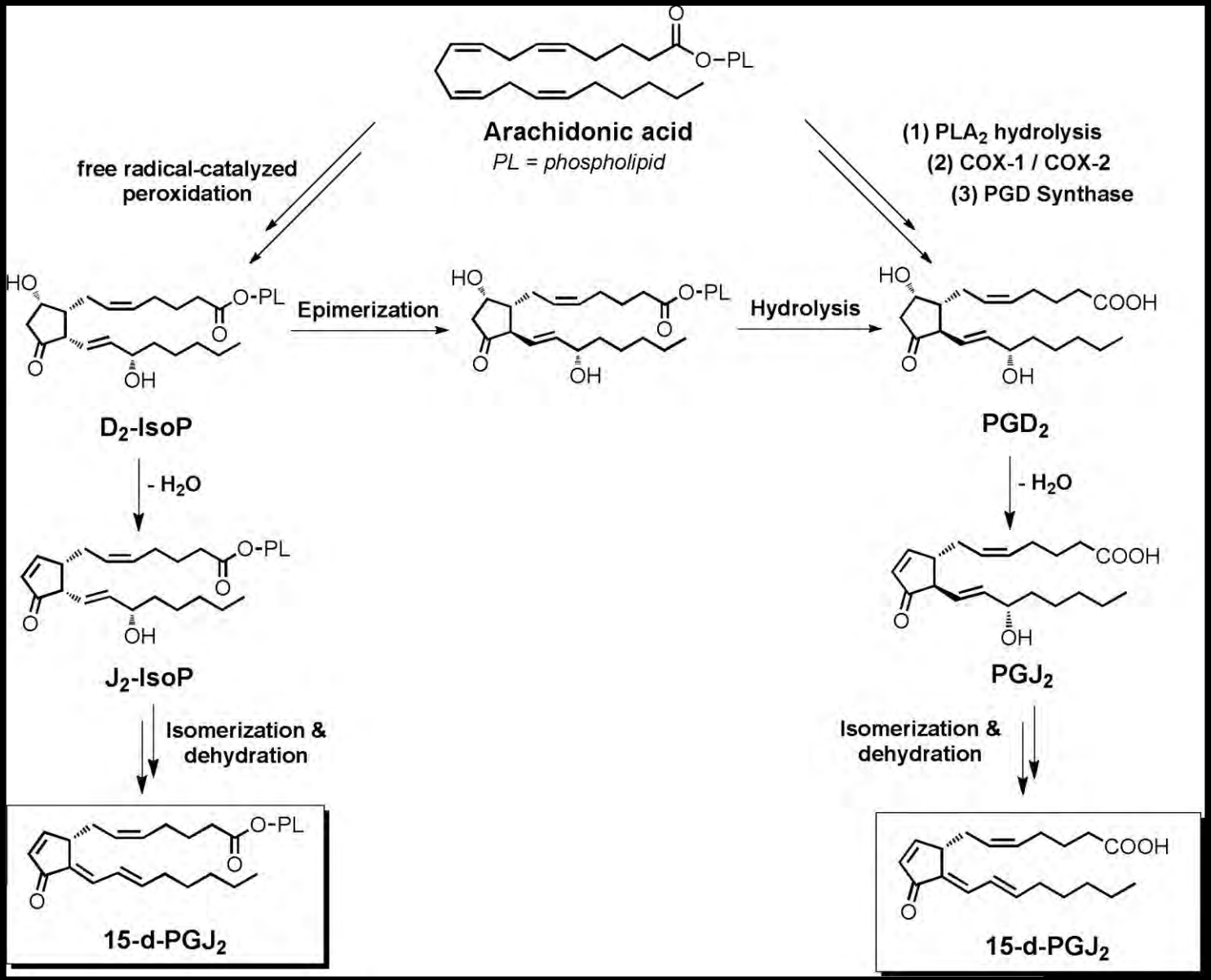
DHA

WAS THE MASTER OF DNA

PART IV

Peroxidation, Altzheimers and special evidence for individual positions in the molecule.

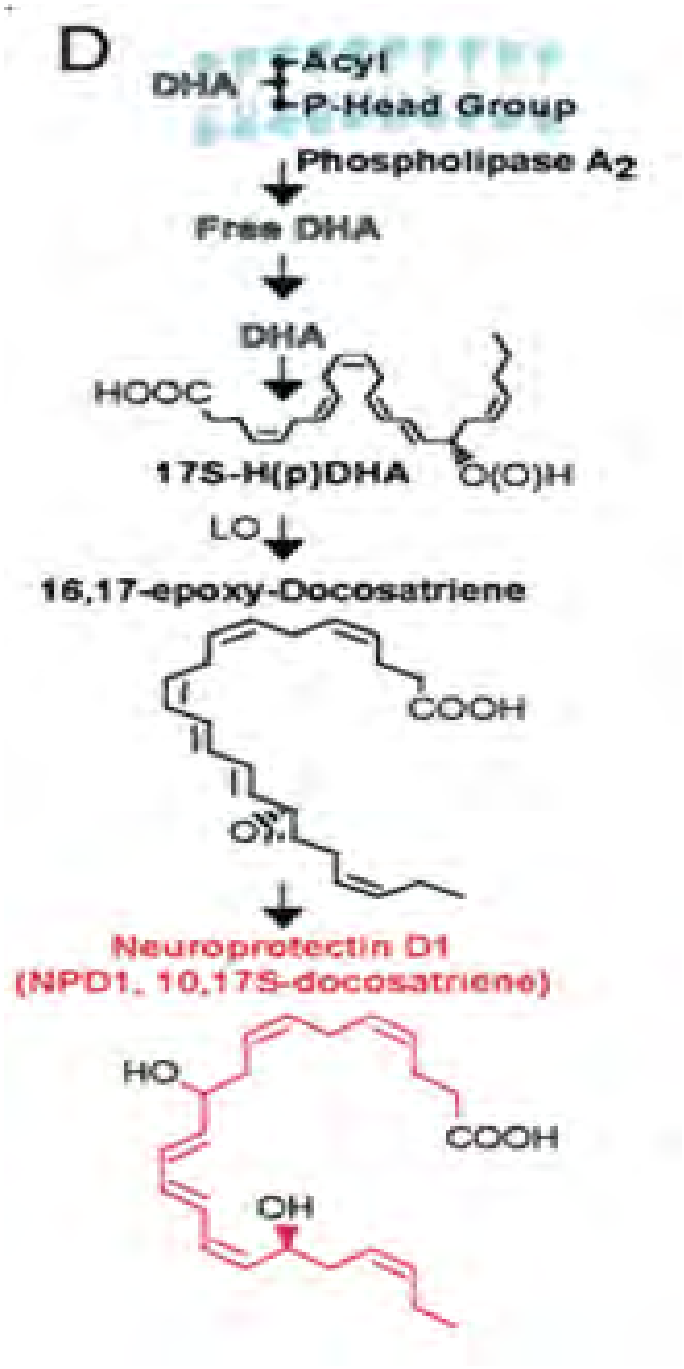

7
10
13
Arachidonic Acid
O
OH
O2
•O–O
5-exo cyclization
more O2
less O2
OO •
HO
IsoFurans
OOH
Isoprostanes


Arachidonic acid
PL = phospholipid
free radical-catalyzed peroxidation
(1) PLA2 hydrolysis
(2) COX-1 / COX-2
(3) PGD Synthase
Epimerization
Hydrolysis
D2-IsoP
PGD2
- H2O
- H2O
J2-IsoP
PGJ2
Isomerization & dehydration
Isomerization & dehydration
15-d-PGJ2
15-d-PGJ2

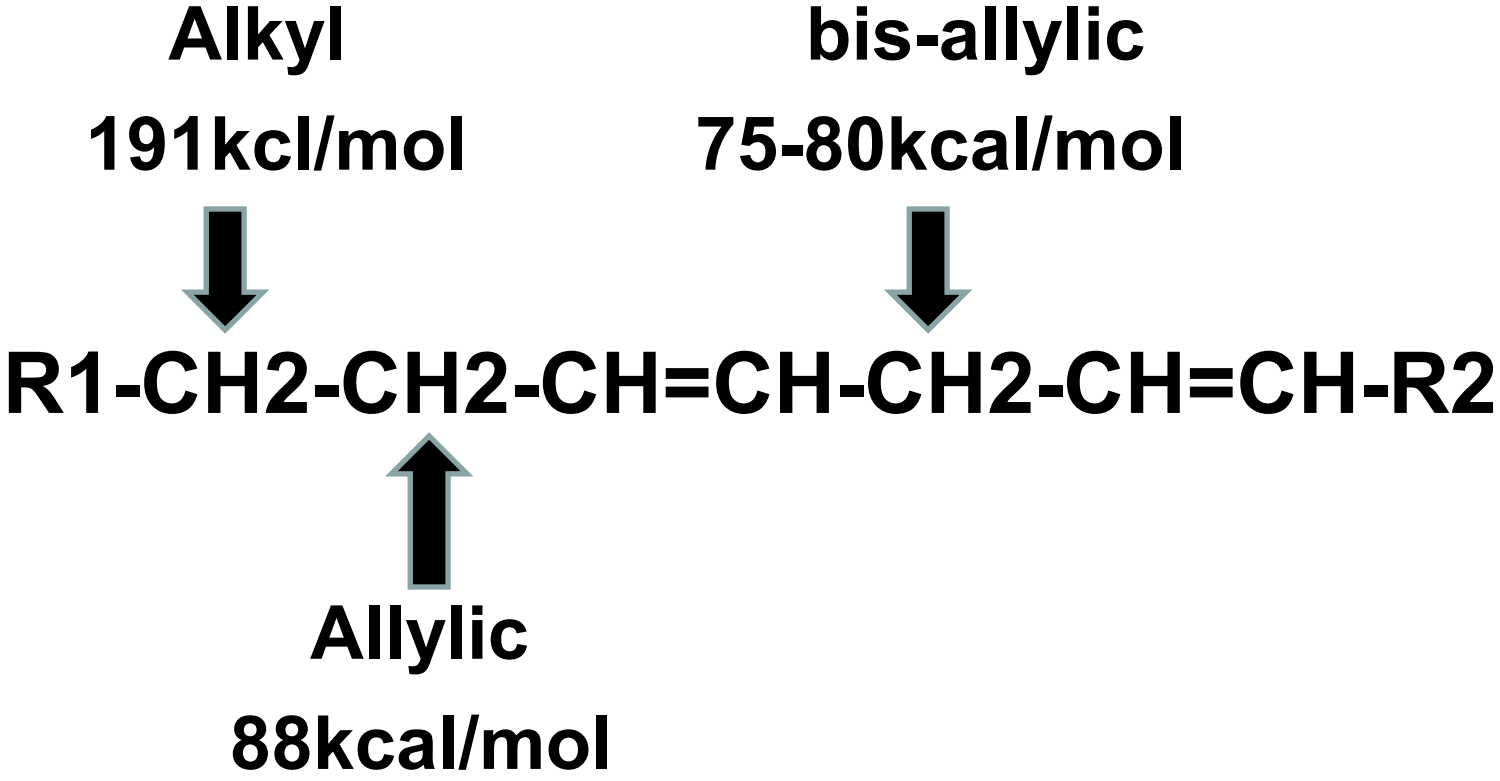
Bazan NG.

Cellular and molecular events mediated by docosahexaenoic acid-derived neuroprotectin D1 signaling in photoreceptor cell survival and brain protection.

Prostaglandins Leukot Essent Fatty Acids. 2009 Aug-Sep;81(2-3):205-11

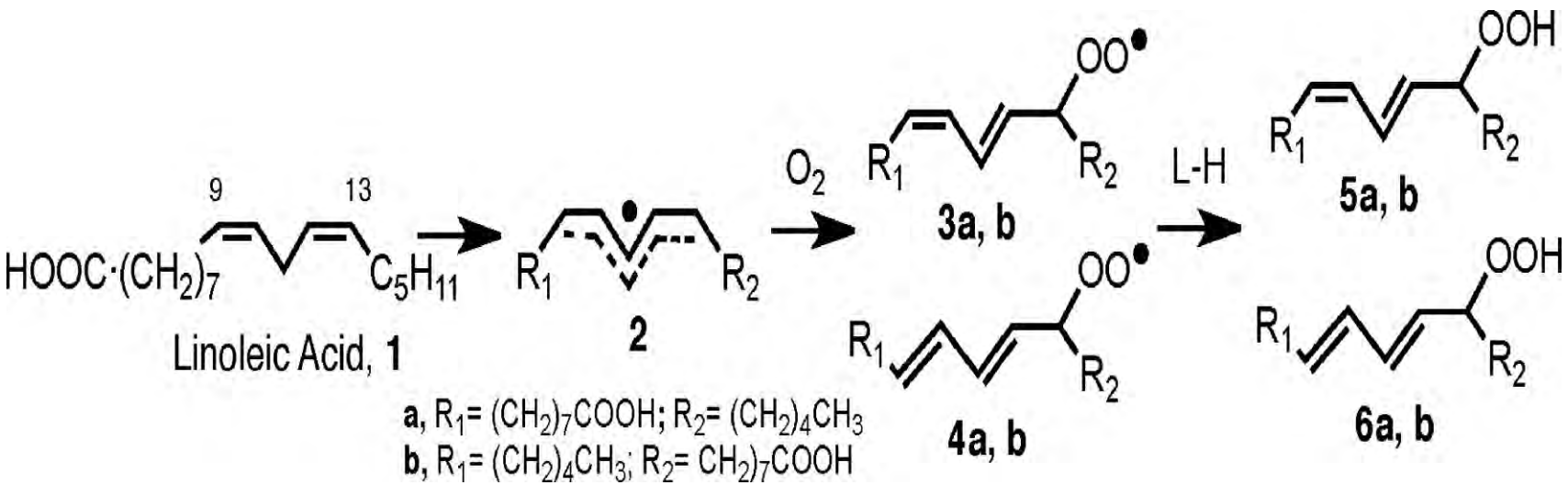


The rate of cellular lipid peroxidation increases exponentially with the number of bis-allylic positions



Brett **A.** Wagner, Garry R. Buettner, C. Patrick Burns JBiochemistry **1994, 33, 4449-4453**

BIS-ALLYLIC OXIDATION OF LINOLEIC ACID.



Published in: Derek A. Pratt; Keri A. Tallman; Ned A. Porter; *Acc. Chem. Res.* **2011,** 44, 458-467.
DOI: 10.1021/ar200024c

Deuterium selectively incorporated into the bis-allylic position inhibits peroxidation.

- An ROS molecule (e.g. a superoxide) may finds itself surrounded by a dense forest of PUFAs; it damages one of them, and a chain reaction follows until the chain hits on an antioxidant and stops.
- Toxic carbonyl compounds (HNE, malonic dialdehyde, and many other) then can leave membrane and do much damage elsewhere.
- PUFAs deuterated at the bis-allylic positions do not sustain the chain reaction, while being otherwise identical to natural PUFAs.

Another example of the uniqueness of lipid intimate structures

- Misha at Retrotope has so far successfully tried the approach in yeast and then in experimental animal models of Parkinson's, Friedreich's, and, most recently, in Diabetic Retinopathy(DR) models.

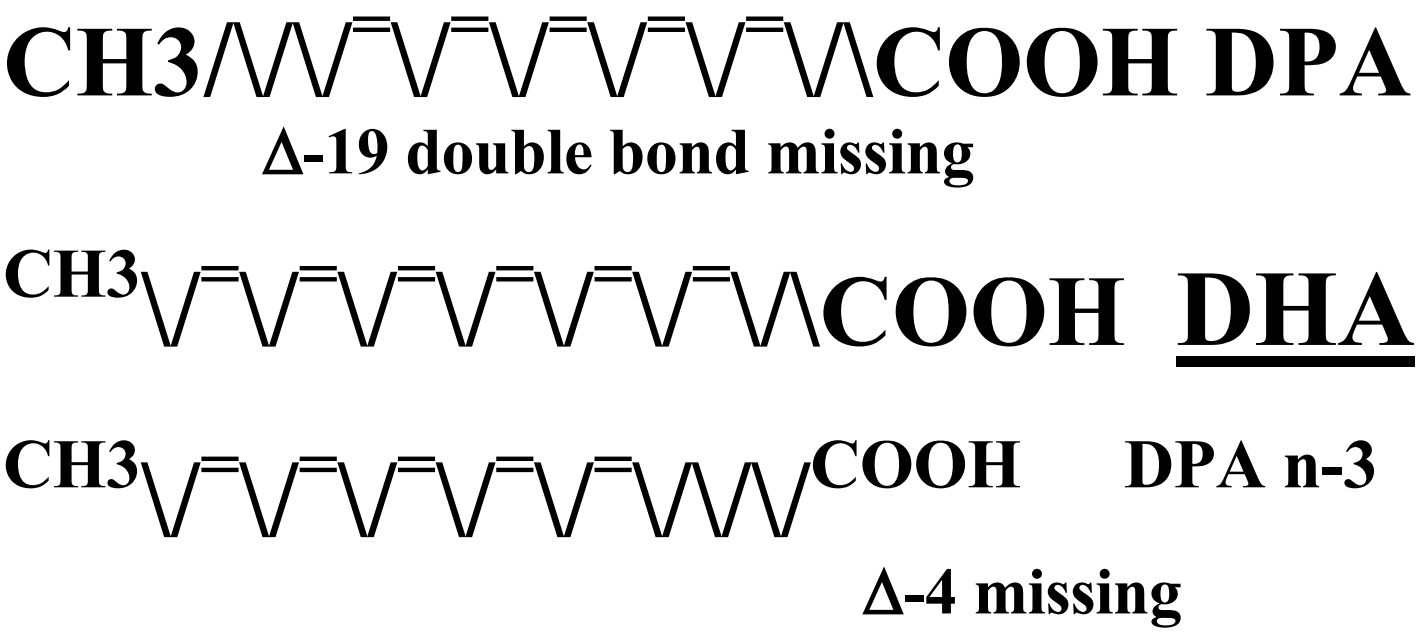
- An example of the structural uniqueness of lipids.

- Incidentally the marine food web, especially at the top is richer in heavy isotopes compared to land foods.

PART V

WHAT IS SPECIAL ABOUT DHA TO EXPLAIN ITS 600 MY TRACK RECORD IN NEURAL SIGNALLING?

WHAT IS SPECIAL ABOUT DHA?
(WHY A 600 million year track record?)



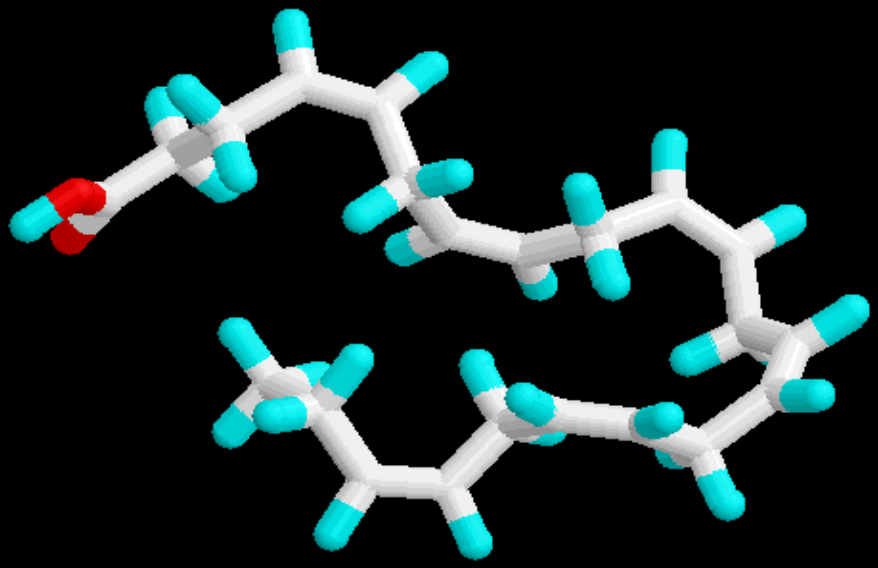
DPA n-3 THE Δ-4 DOUBLE BOND IS OMITTED

DPA n-6 THE Δ-19 DOUBLE BOND IS MISSING

Although the n-3 DPA is a precursor for DHA neither DPA replaced DHA in 500 million yrs of evolution . so these two double bonds may be critical to DHA's role in signaling membranes.

Docosahexaenoic acid

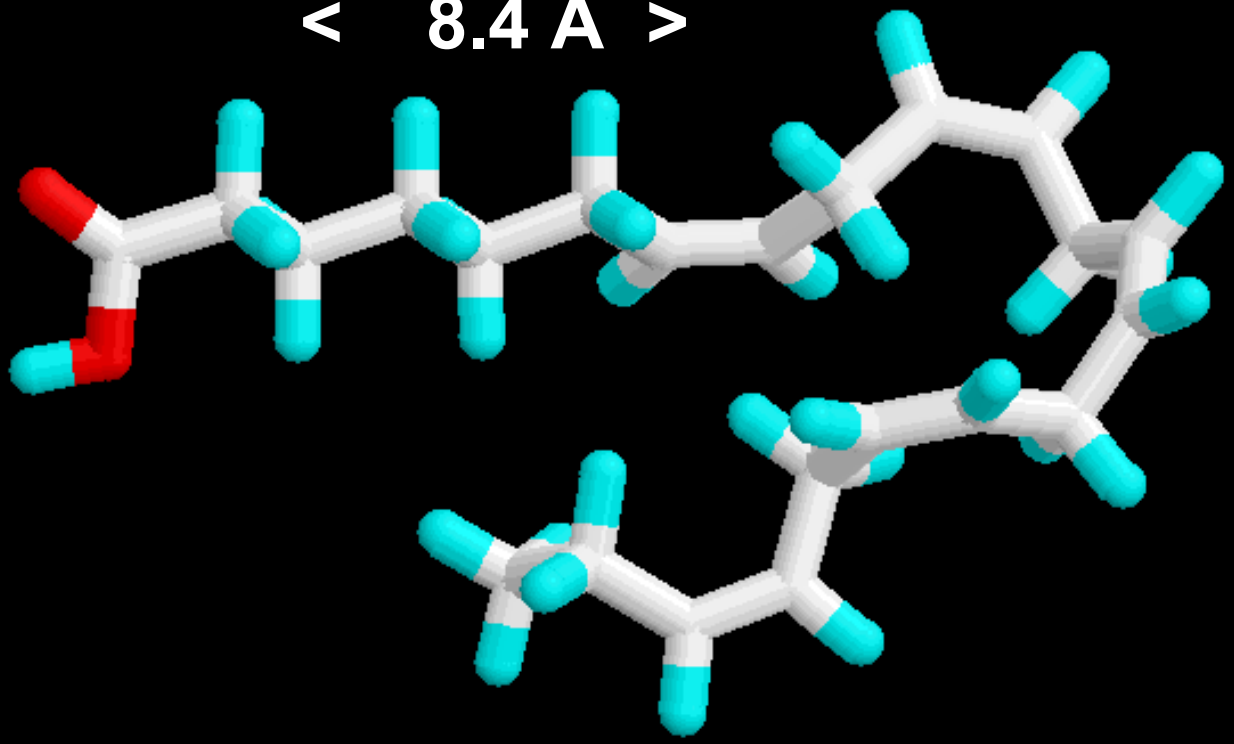
Alchemy optimized conformation:
double bond 1,3, 6 planar and π–π orbitals co-planar



The planar-ness of the preferred DHA conformation is a fundamental characteristic of the six double bonds separated by CH2 groups. If there are only five, the corresponding molecule cannot be made planar.

n-3 DPA odd number of double bonds and 1, 5 planar

< 8.4 Å >



<4.2 Å >

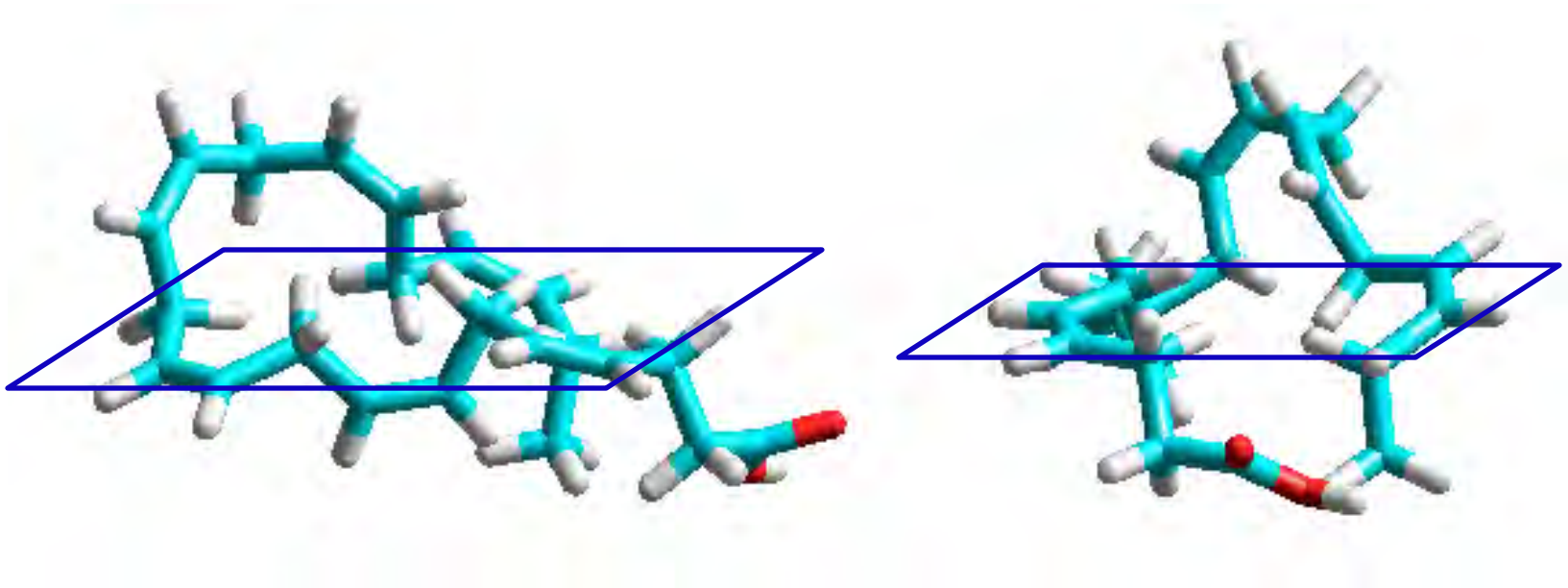
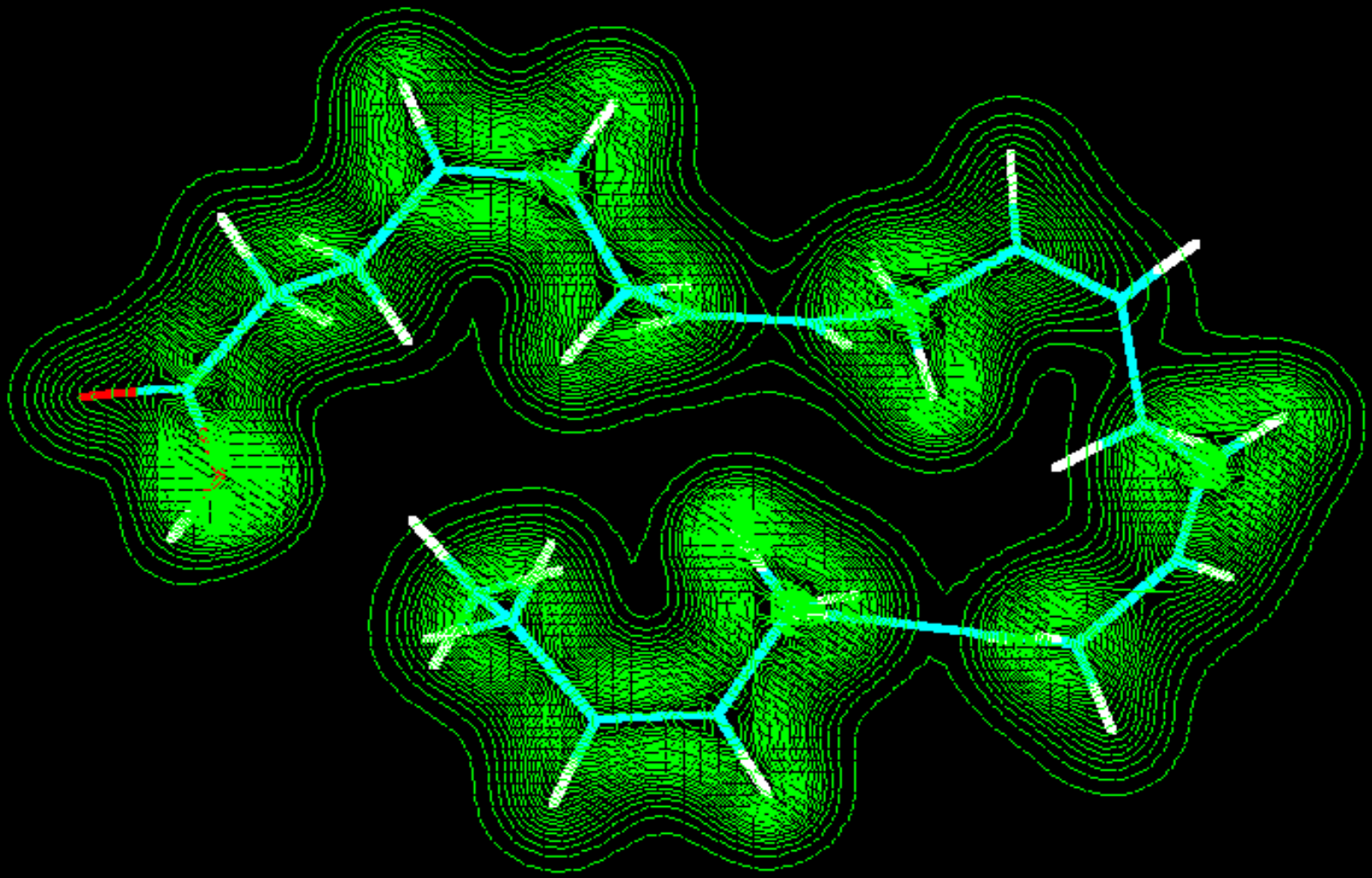


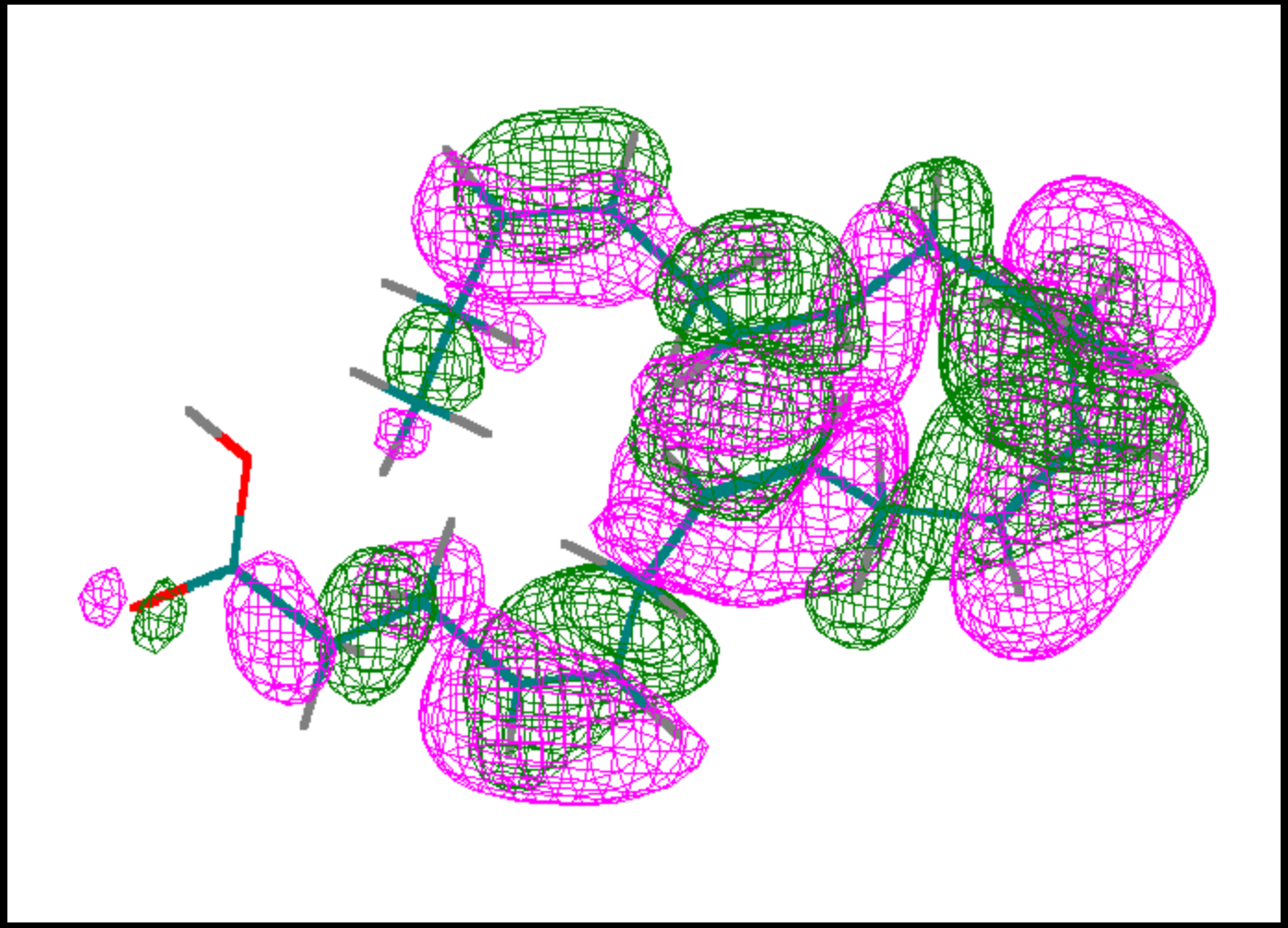
Figure 2. Co-planar C-CH=CH-C groups (1, 3 and 6).

2 Dimensional - Charge Density
(3 double bonds coplanar)



Least Unoccupied Molecular Orbitals - LUMO

(π bond energy different above and below planes; green lower, mauve higher energy)



Alternative positive-negative sets the stage for semi-conduction.

Hypothesis: Potential of DHA to act as a semiconductor contributing to electrical properties of signalling.

Calculations based on the least occupied orbitals for DHA show that the bonds have + and - lobes and that the + and – signs of orbitals of the two different hydrogens on the CH2 groups also have + and – signs related to (typically opposite to) the signs of the adjacent π bonds.

This is a simple mechanism to explain electron coherence over a large distance, even though the double bonds are not extended resonance structures across a sequence of carbons. None of this works with DPA which has one double bond missing leading to a saturated chain too long for tunnelling.

Nuclear Overhauser Enhancement an NMR technique to detect the potential for electrical function demonstrates the feasibility of electron responses within DHA. These slides have been removed because of their large memory capacity but will be published in the PLEFA.

The methylene interruption of the π-electrons is crucial. It denies the copper wire like electron transfer in a conjugated sequence

(-CH=CH-CH=CH-CH=CH-) as in retinal. In the conjugated system, the π-electron clouds can overlap allowing electron (current) flow.

However, the **–CH2-** is an electrical resistor but its

Polarisation in DHA is critical and offers a plausible key to the uniqueness of DHA in signalling .

The π-electrons on the CH=CH groups are localized by the presence of the –CH2– barriers. The classical notion of such an energy barrier conjures a notion of a brick wall over which you have to have enough energy to jump over it.

However, in quantum mechanics there is no such wall. There is only an electro-magnetic force holding electrons in orbit and a probability of its location. Hence there is a probability that it will penetrate the barrier..

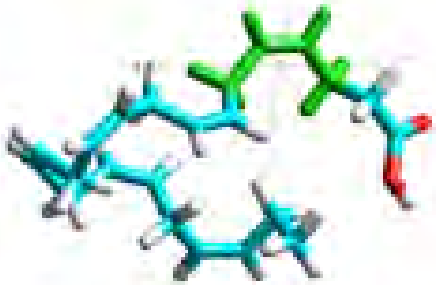
Pauli Exclusion Principle provides quantum precision in the signal.

- If one electron is de-localised and pulled through the barrier (tunneling) by a sufficiently strong +ve to –ve difference (hyperpolarization) across the membrane then an immediately distal electron will tunnel to take its place and lead to a current to flow and depolarization.
- No two electrons can occupy the same energy state. If one electron is pulled out, it leaves a hole in the outer orbit which can only be filled by an incoming electron.
- The hole can only be filled with an electron of the precisely the same spin and energy.
- This process could theoretically depolarize the membrane and moreover do so *only at a single and precise energy level*.
- This is a plausible explanation for the absolute precision of the depolarization and the high degree of visual acuity.

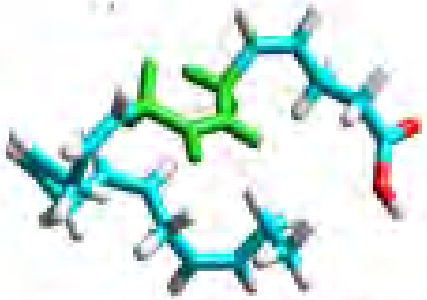
Quantum mechanics of ET can explain currently unexplained phenomena. Precision of energy transfer explains how:

- The system capable of responding over a range of 1-10,000
- Activation by a single photon always produce the identical response regardless of the energy of the photon which is unexpected from the conventional story.
- The photoreceptor faces opposite to incoming light as a wave.

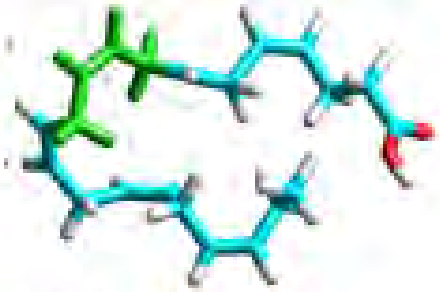
MOMENTS OF INERTIA ACROSS DHA DBs



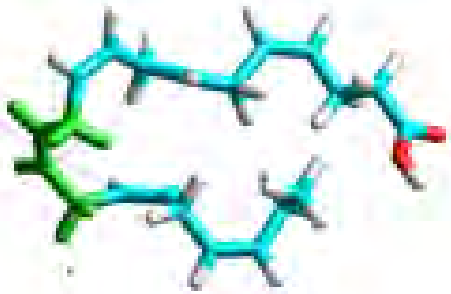
Moments of inertia: 29.186 ; 85.9286 ; 11



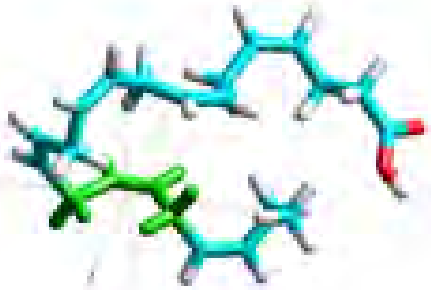
31.471 ; 80.9784 ; 107.954



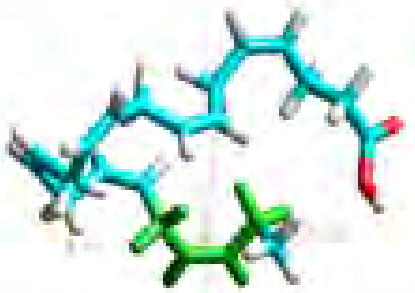
28.831 ; 85.5551 ; 112.353



Moments of inertia: 28.831 ; 85.5551 ; 112.353



31.471 ; 80.9784 ; 107.954



28.8925 ; 85.6158 ; 112.499

Physical properties of DHA

- The torsional energy is especially reduced by the CH2 interruption, this reduces torsional resistance allowing special flexibility.
- Gawrisch K., Eldho N. V. and Holte L. L. (2003) The structure of DHA in phospholipid membranes. Lipids 38, 445–452.

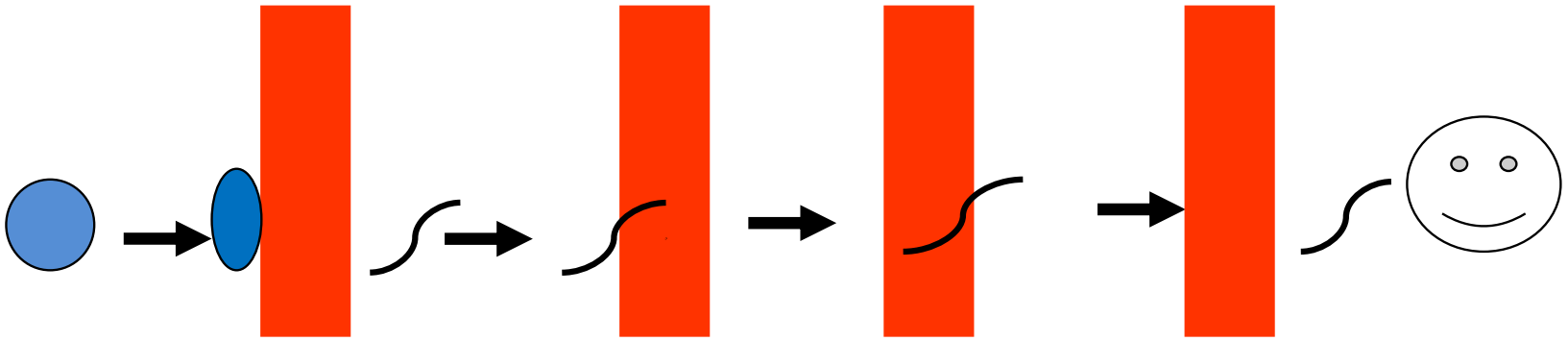
The Photoreceptor and its π electrons

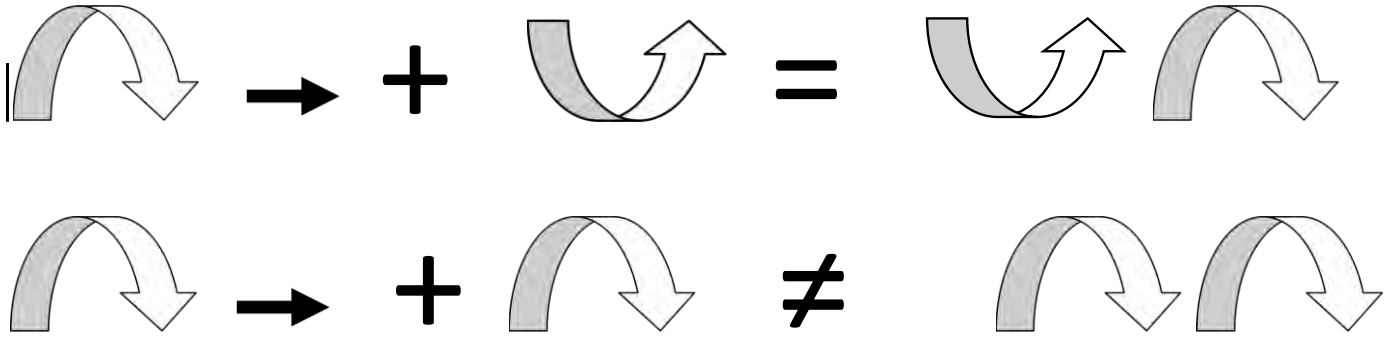
- Einstein 1905 – photo-electric effect $E = hv$.
- An electron energised by a photon is raised to a higher orbit. If the energy is sufficient it leaves the orbit and creates a current.
- The isomerization of retinal is achieved by the electron energised by a photon, leaving the 11-cis oribit. The resultant single bond recaptures the electron falling into the trans configuration which activates rhodopsin.
- So might a photon energise an electron on the adjacent DHA?

ELECTRON TUNELLING: THE DUAL PROPERTIES OF THE ELECTRON

A quantum mechanical explanation for 600 my exclusive use in neural signalling.

δ [– VE] δ [+ VE]





Pauli exclusion principle: same spin and E forbidden.

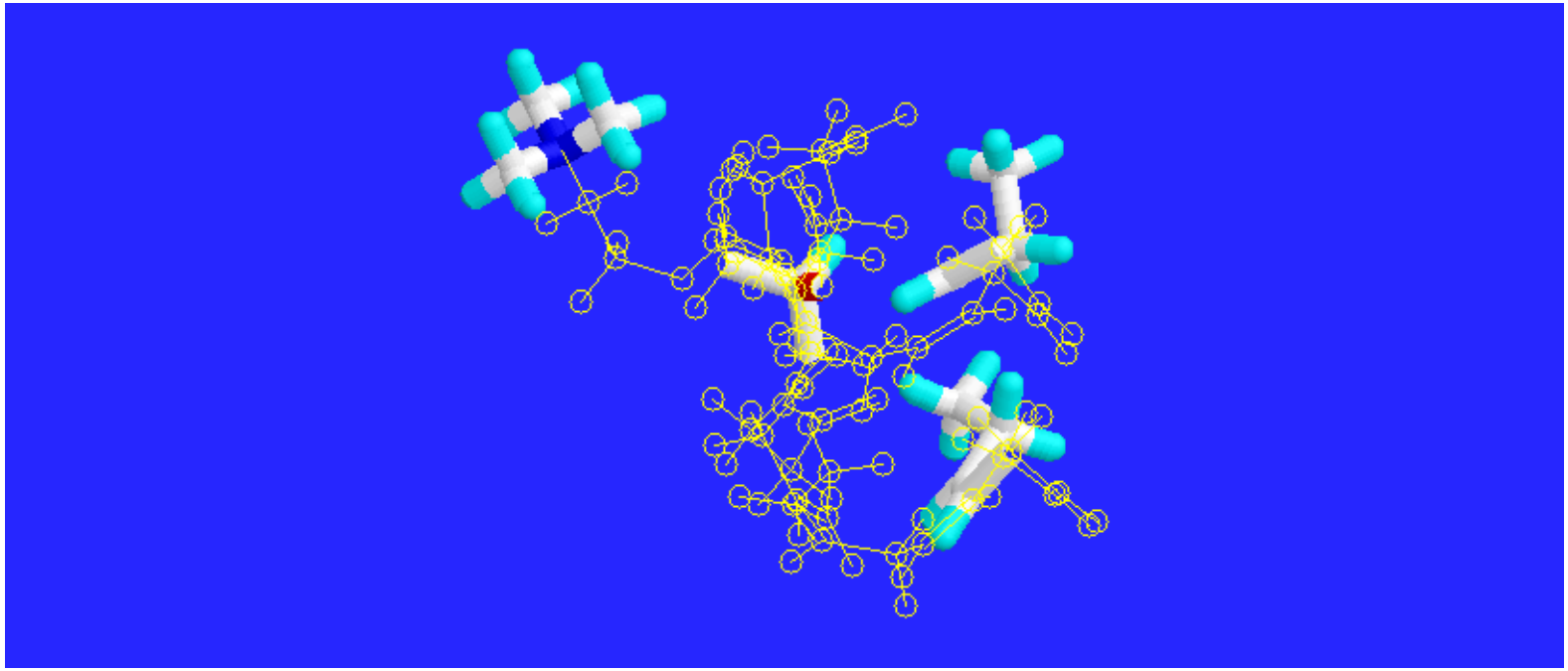
If **E > Ee** the current flows at **Ee.** If **E < Ee** no current flows. If **E >>> Ee** current still flows at **Ee**

Double slit explanation for the upside down photoreceptor.

The Young double slit behaviour: if a photon is fired at a screen with two slits, you might expect its transit as a particle will make it go through one or another. It does not. Instead it produces an interference pattern. This result demonstrates the wave like behaviour of the photon. By presenting the back end of the receptor (slide 10) the forest of back-ends establishes the wave function of the photon ensuring the energy captures a sensitive region as in the excitation of the cis π electron in retinal which initiates its isomerization and the rhodopsin triggered signaling cascade that shuts down the dark current and results in hyperpolarization of the membrane. Wave lengths of visible light range from about 380 nanometers (nm = 1×10^{-9} m) to about 740 nm. An Angstrom unit is (1×10^{-10} m). A particle might miss!?

di-DHA-phosphatidylcholine molecule viewed perpendicular to the plane

Sites of build-up: Terminal N methyl group, CH glycerol carbon, and two terminal **C**H3**C**H2-**C**H=**C**H groups. Note remaining double bonds are planar.

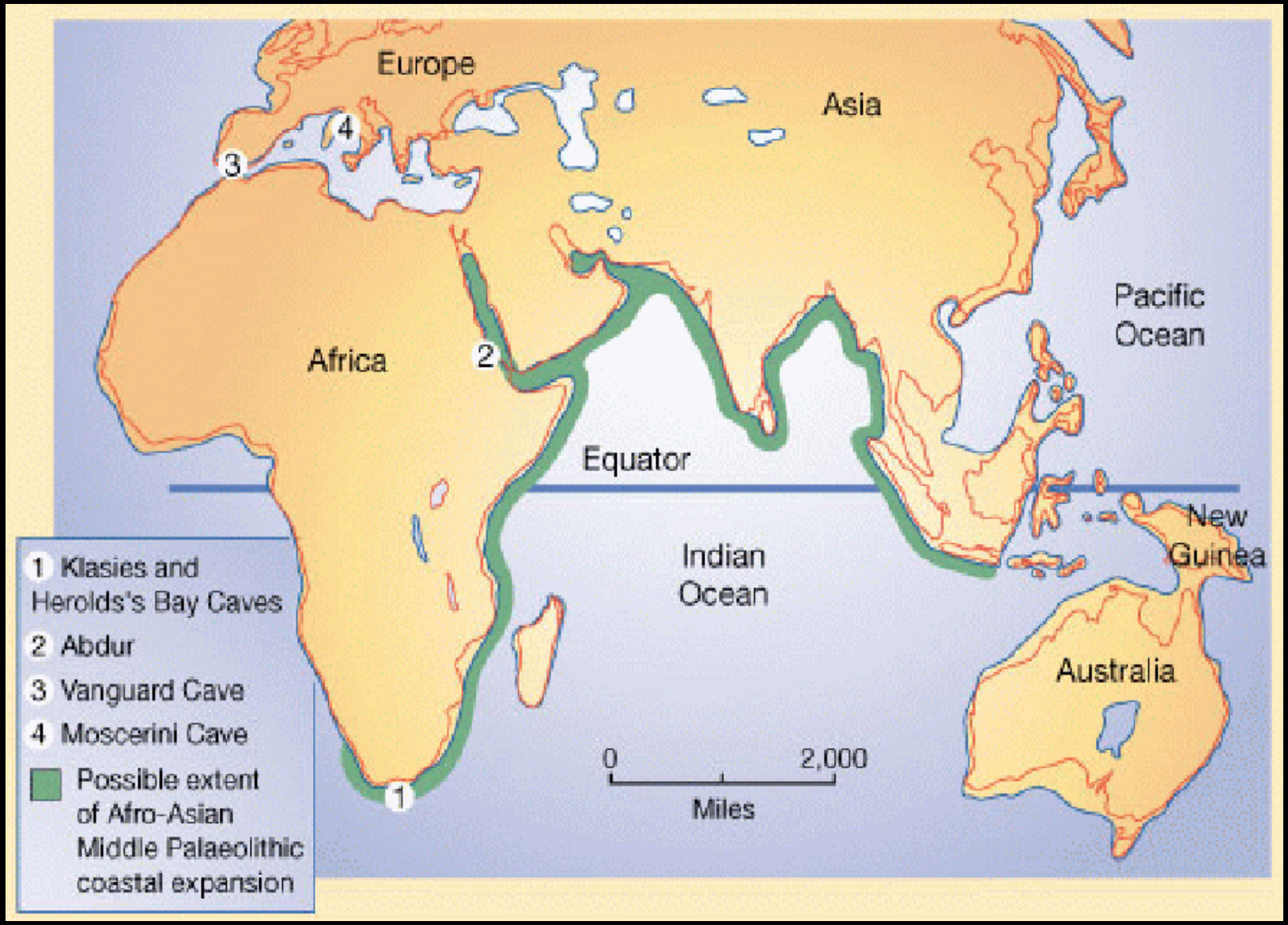


(CH3)3-N has a partial +ve charge, and the two CH3CH2CH= groups have a partial more negative charge, a mechanism exists for polarization to build up above and below the plane with the potential Semi-conduction.

- Whist further investigation is needed to test this feasibility, photo excitation of a π- electron in DHA is an attractive addition to the ET hypothesis. Ċalculation indicates the potential of the molecule to respond to visible light.
- At the synapse, the hyperpolarized membrane may be sufficient the suck an electron out of orbit. .
- Examples of this activity would be the DHA involvement in signalling in hippocampal cells and cardiac myocytes described by Alex Leaf.
- The quantum mechanical considerations presented here do not prove that electron tunnelling is the secret to the success of DHA over the 600 my of animal evolution. It simply demonstrates the feasibility.

PART V

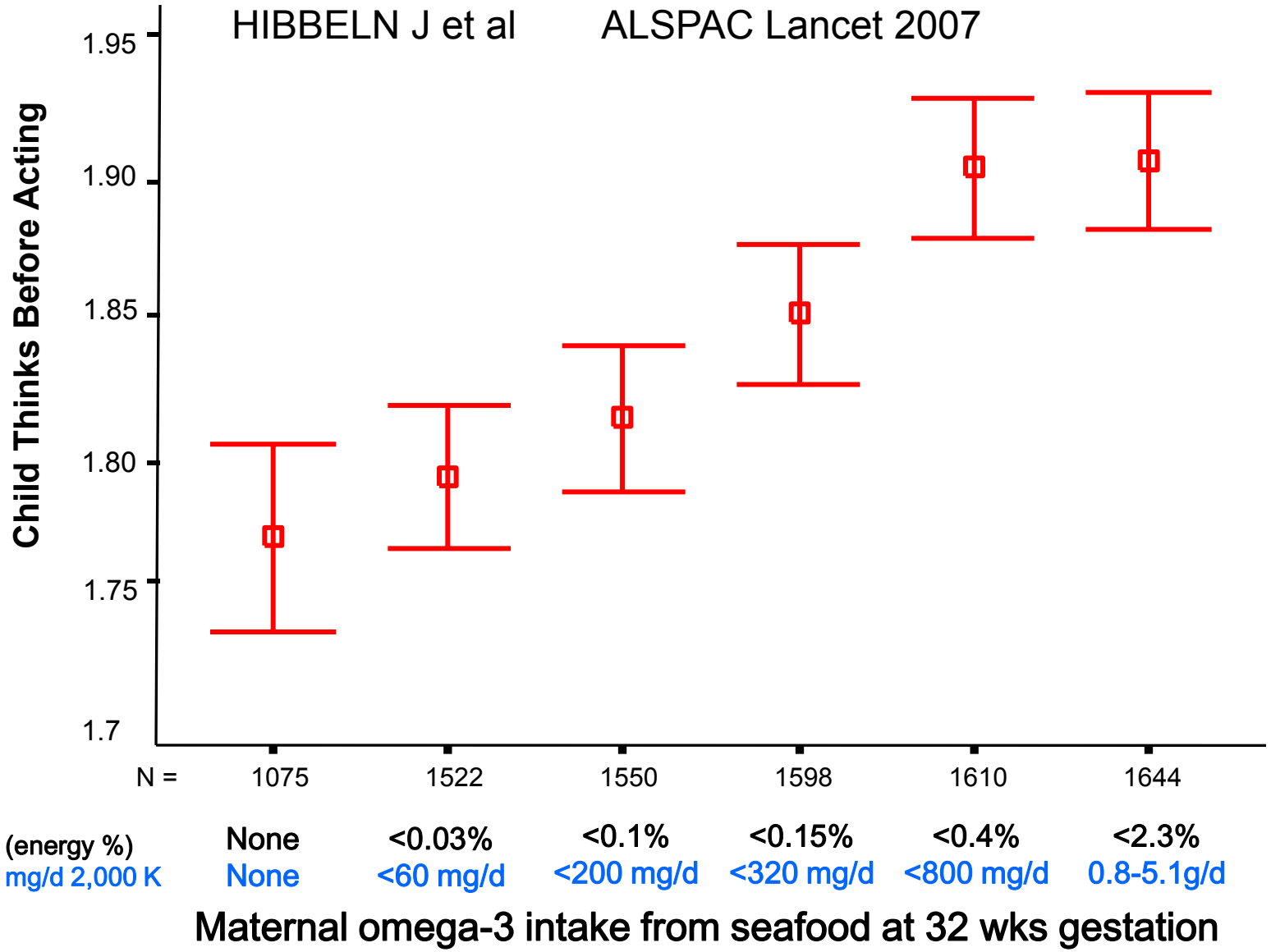
MARINE FOOD WEB AND THE PAST AND FUTURE OF H. SAPIENS.



Out of Africa: ***Stringer C. (2000) Palaeoanthropology. Coasting out of Africa. : Nature 2000 May 4;405(6782):24-5, 27***

Weighing no more than a bag of sugar this infant has an 80% chance of severe brain injury

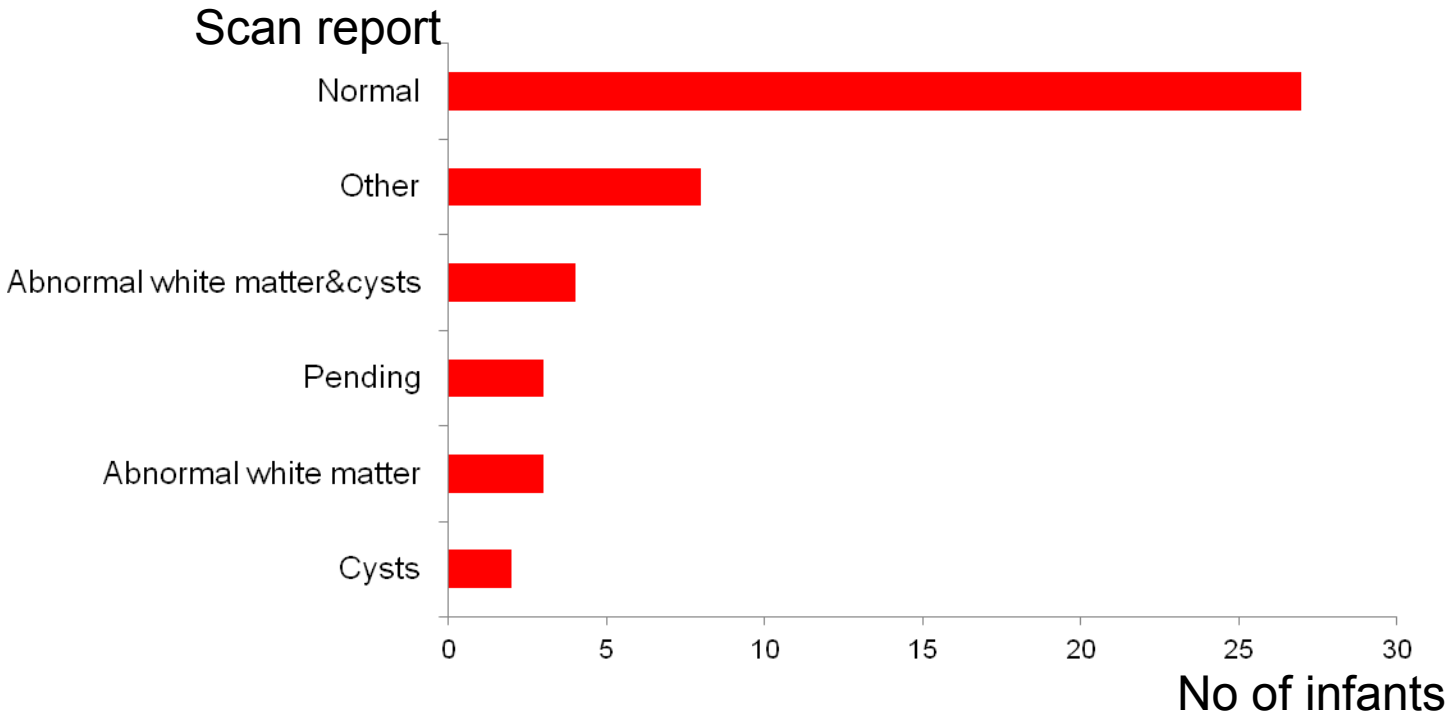
ALSPAC: Child thinks before acting (8 y) and Omega-3 intake by mother in pregnancy (32 w)



Imperial College London

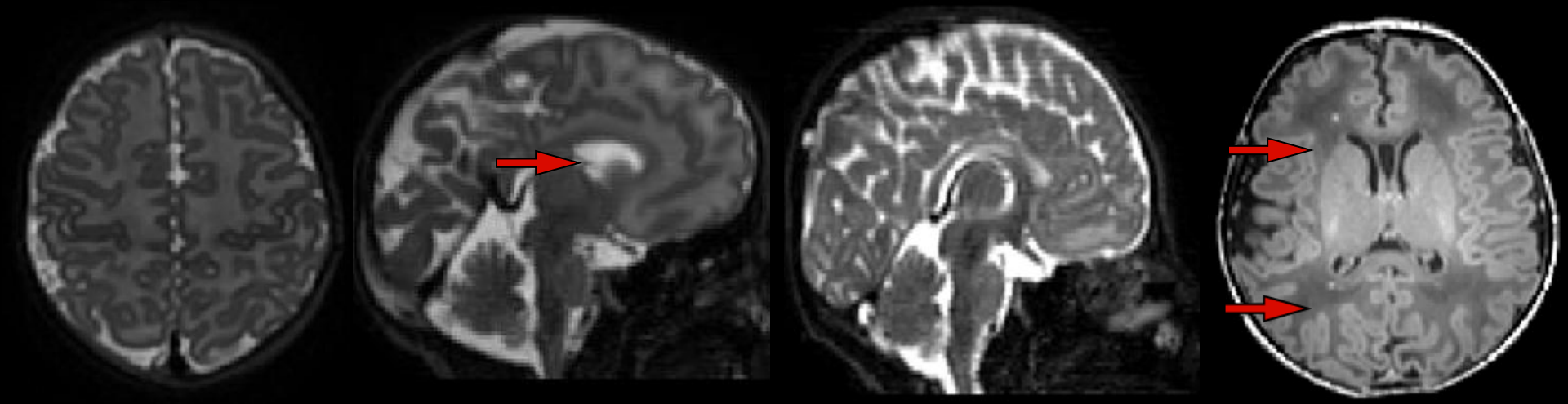
MRC Clinical Sciences Centre

Brain MRI scan at term age – Scan results
First 56 infants.



Current work on MRI scans at birth of allegedly normal infants. Cyst shown below. Also we see deep venous anomalies in 9/42 (<1% reported in adults).

Normal Cyst (arrow) - white matter altered signal intensity - punctate lesions

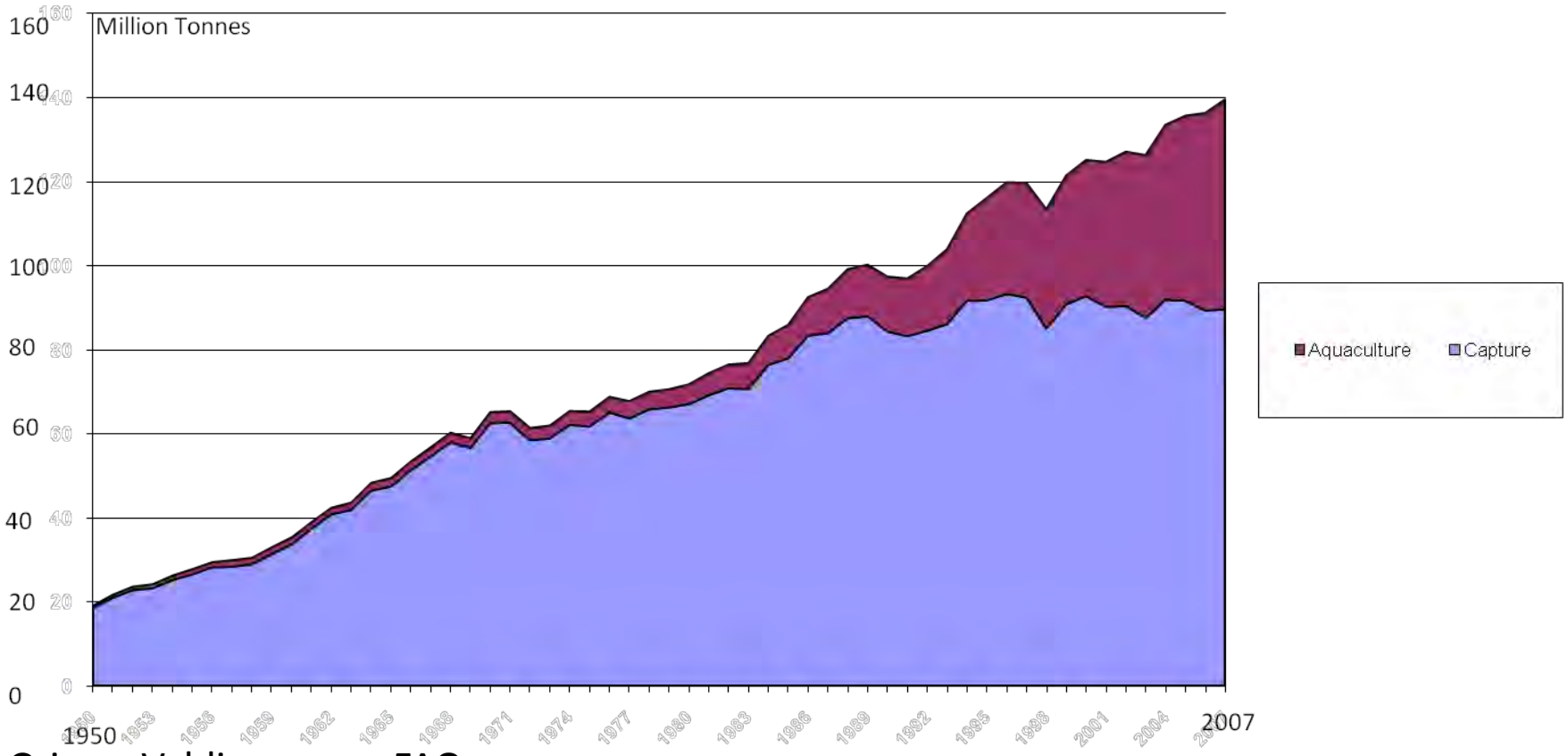


22% in preterm infants

Conclusion: poor maternal/fetal nutrition leads to a permanent diturbance of regional brain development with consequences for mental ill health, cognitive, learning and behavioural deficits with risk oif dementias later.

World capture & aquaculture production.

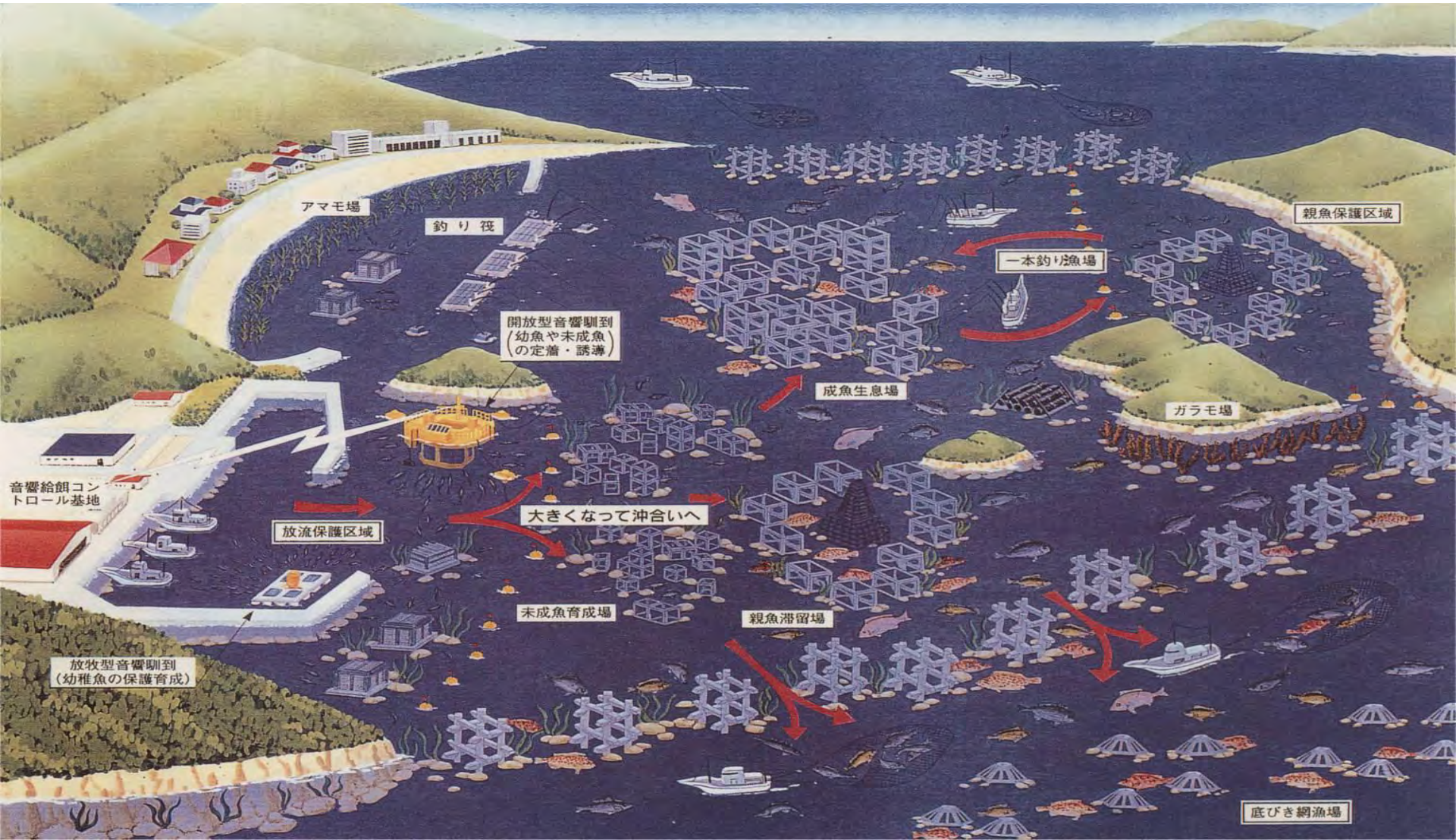
Aquaculture of carnivorous fish depends on the wild catch and thus is limited.



Grimur Valdimarsson FAO

SOLUTION: MARINE AGRICULTURE

Shiraishijima Island, Japan (Dr. T. Tanaka),



LAND - GREEN PASTURE

Marine Pasture Development (Dr. T. Tanaka)

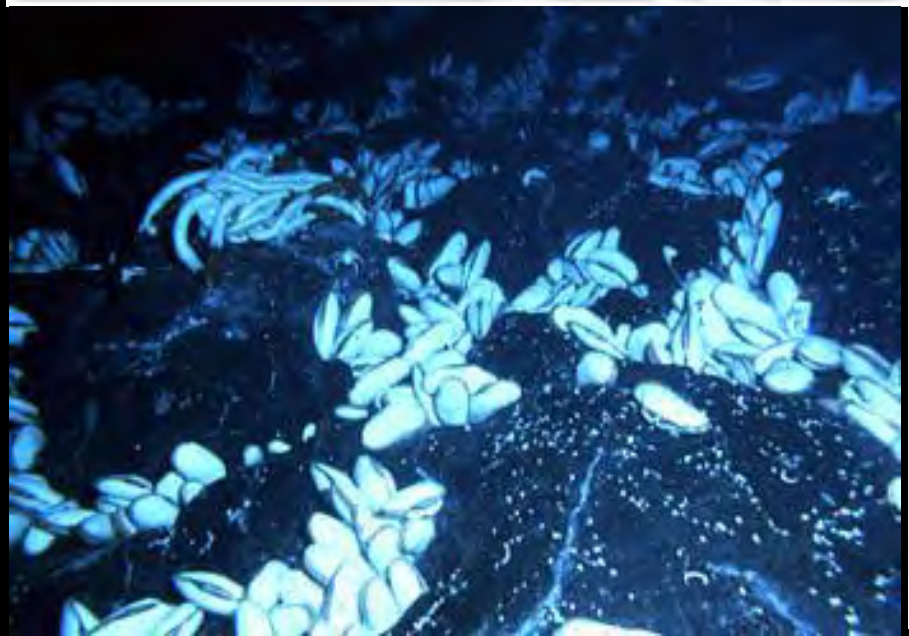
Eel Grass (Zostera marina)

Geothermal vents inject iron, manganese especially but also a wide range of trace elements contributing to the local food web and ultimately to the web at the upper levels.

Giant tubeworms can grow to 2.4 m (7 ft 10 in)[1] tall because of the richness of nutrients.
By now, over 300 new species have been discovered at hydrothermal vents.
Little is known about the deep sea food web which will be significant as it supports the growth of the giant squid.

Without light, whale falls etc provide an important source of nourishment.

Life at the hydrothermal vents



Sea Bed Kelp Farming –Bali, Indonesia

Conditions of existence:

Rise in Brain disorders

EU - 2004 €386 Billion 2010 € 789 Billion

UK 2007 £77 Billion : Greater than heart disease and cancer combined.

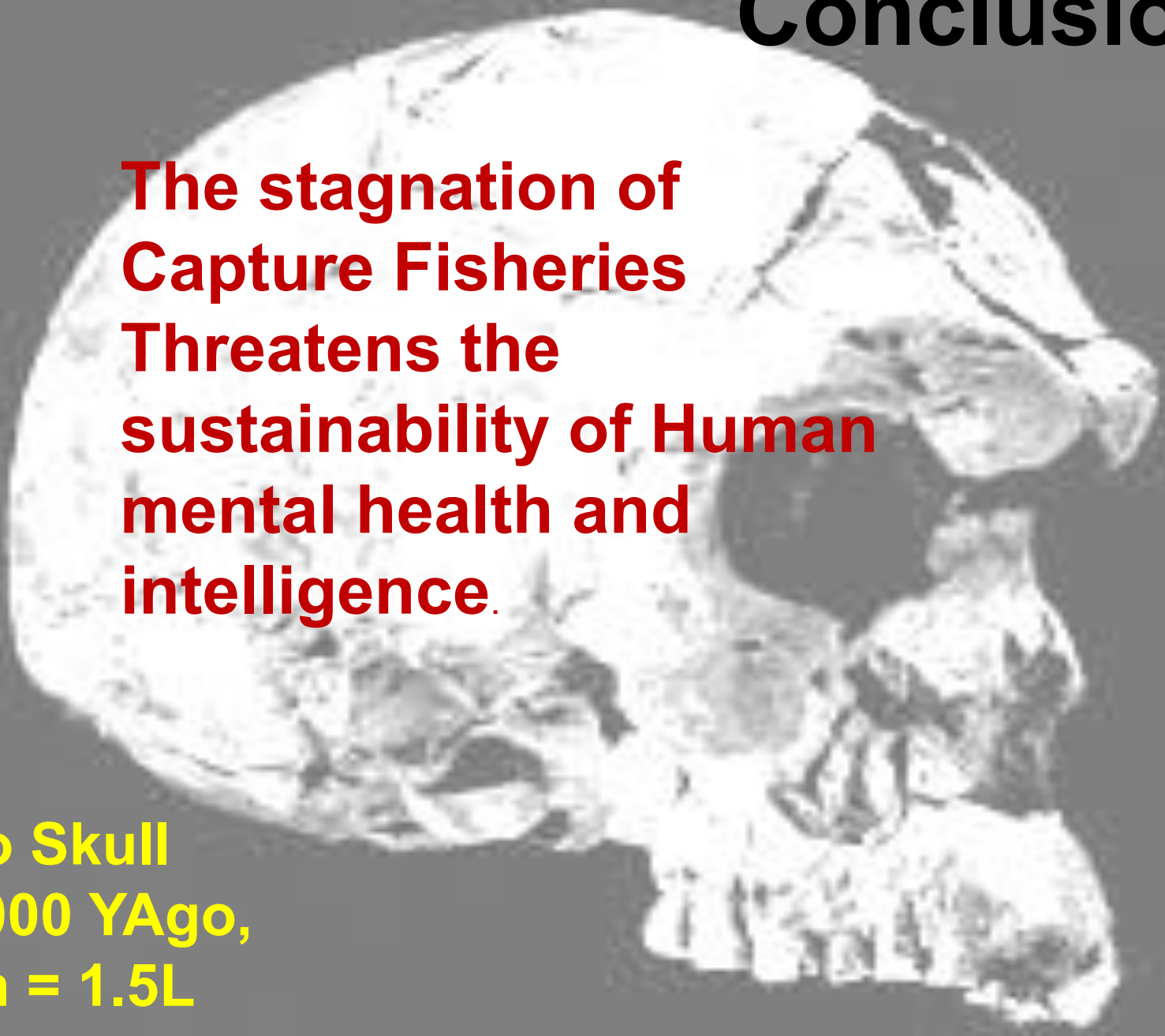
2010 £105 Billion

USA £386 Billion

WORLD: No 2 Burden of health world wide by 2020.

Another 1 billion people in 12 years time.

Conclusion



The stagnation of Capture Fisheries Threatens the sustainability of Human mental health and intelligence.

Herto Skull
160,000 YAgo,
Brain = 1.5L

THE BRAIN EVOLVED IN THE OCEANS 500 MILLION ya. IT STILL DEPENDS ON THE SAME SEA FOOD. WE ARE RUNNING OUT OF TIME: THAT MEANS MARINE AGRICULTURE.

THANK YOU

Collaborators

- **Myer Bloom – Physics, Vancouver, Canada**
- **Annette Brand, Q-Tof, Weizmann Institute, Israel***
- **Leigh Broadhurst – Geophysics & Paleoanthropology, USDA*.**
- **Stephen Cunnane –Neurodegeneration, Sherbrooke, Canada.**
- **Keb Gebremeskel – Lipidomics, London Metropolitan, UK.**
- **Martin Guest, Liverpool Hope University, UK ***
- **Laurance Harbige - Immunology Greenwich, UK**
- **Holm Holmsen – Membrane signalling Bergen, Norway**
- **David Marsh, evolution researcher, London.**
- **Atulya Nagar, Liverpool Hope University, UK ***
- **Enitan Ogundipe, Imperial College, London, UK***
- **Walt Schmidt, MD, NMR, USDA, Beltsville.***
- **Nora Tusor, Imperial College, London, UK***
- **Hiramitsu Suzuki – Synaptic uptake of DHA, NFRI, Japan**
- **Yiqun Wang – Lipidomics, London Metropolitan University UK.**
- **Ephraim Yavin – neuronal migration, Weizmann Institute, Israel***

* Specifically involved in the work involved in this presentation